

# WEST Search History

DATE: Saturday, March 23, 2002

<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
side by side			result set
<i>DB=USPT; PLUR=YES; OP=OR</i>			
L22	L21 or l20	12	L22
L21	L20 and l18	10	L21
L20	L19 and l16	12	L20
L19	vascular near6 (NO or nitric oxide)	1831	L19
L18	L17 and l16	53	L18
L17	endothelium	5393	L17
L16	L15 and l8	336	L16
L15	L14 and l4	336	L15
L14	L13 and l1	336	L14
L13	sustained near5 matrix	1186	L13
L12	L11 and l10	1172	L12
L11	tablet	86472	L11
L10	L9 and l6	2196	L10
L9	L8 and l5	4656	L9
L8	NO or nitric oxide	2438718	L8
L7	L6 and l5	2197	L7
L6	matrix	217631	L6
L5	L4 and l1	4670	L5
L4	L3 or l2	76897	L4
L3	sustained or extended near5 (release or released or releasing)	58361	L3
L2	controlled near5 (release or released or releasing)	24697	L2
L1	arginine	24821	L1

END OF SEARCH HISTORY

=> d his

(FILE 'HOME' ENTERED AT 16:30:50 ON 23 MAR 2002)

FILE 'REGISTRY' ENTERED AT 16:30:57 ON 23 MAR 2002

E ARGININE/CN

L1 2 S E3

FILE 'CAPLUS, USPATFULL, WPIDS, MEDLINE, BIOSIS, SCISEARCH, DRUGU, DRUGLAUNCH' ENTERED AT 16:32:34 ON 23 MAR 2002

L2 73858 S L1  
L3 129991 S (CONTROLLED OR SUSTAINED OR EXTENDED) (6A) (RELEAS#####)  
L4 261 S L2 AND L3  
L5 7452226 S NITRIC OXID## OR NO  
L6 82 S L5 AND L4  
L7 222939 S ENDOTHELIUM  
L8 49 S L7 AND L4  
L9 41 S L6 AND L8  
L10 38 DUP REMOVE L9 (3 DUPLICATES REMOVED)

=> d 14 225-247 bib,ab

L4 ANSWER 225 OF 261 MEDLINE  
AN 94282474 MEDLINE  
DN 94282474 PubMed ID: 8012717  
TI Prevention by insulin treatment of endothelial dysfunction but not enhanced noradrenaline-induced contractility in mesenteric resistance arteries from streptozotocin-induced diabetic rats.  
AU Taylor P D; Oon B B; Thomas C R; Poston L  
CS Division of Physiology, United Medical School Smooth Muscle Group, London.  
SO BRITISH JOURNAL OF PHARMACOLOGY, (1994 Jan) 111 (1) 35-41.  
Journal code: B00; 7502536. ISSN: 0007-1188.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199407  
ED Entered STN: 19940810  
Last Updated on STN: 19940810  
Entered Medline: 19940725  
AB 1. Streptozotocin-induced diabetic rats (Wistar) were implanted with **sustained release** insulin pellets (**release** rate = 4 u day<sup>-1</sup>) or with placebo pellets (palmitic acid) from the onset of glycosuria. 2. Noradrenaline sensitivity, endothelium-dependent relaxation to acetylcholine and endothelium-independent relaxation to sodium nitroprusside were assessed in mesenteric resistance arteries from the insulin-treated (IT) diabetic animals and compared to placebo-implanted (PI) diabetics and age-matched controls. 3. Arteries from PI-diabetic rats (8-10 weeks) demonstrated an enhanced maximal response to noradrenaline compared to controls, which was not prevented by insulin treatment (control 2.65 +/- 0.17 mN mm<sup>-1</sup>, n = 18 arteries versus PI-diabetic 3.73 +/- 0.40 mN mm<sup>-1</sup>, n = 5, P < 0.05; control versus IT-diabetic 4.02 +/- 0.19 mN mm<sup>-1</sup>, n = 22, P < 0.001). Sensitivity to noradrenaline was similar between the three groups. 4. In the presence of the nitric oxide synthase inhibitor NG-nitro-L-arginine methyl ester (L-NAME), IT and PI arteries were more sensitive to noradrenaline than control arteries (pEC<sub>50</sub>: control 5.75 +/- 0.08, n = 17, versus PI-diabetic 6.14 +/- 0.09, n = 8, P < 0.05; control versus IT-diabetic 6.38 +/- 0.08, n = 20, P < 0.001). 5. The maximum contractile response to depolarizing 125 mM K<sup>+</sup> was significantly enhanced in IT-diabetic arteries but not PI-diabetic when compared to control arteries (maximum response: control 3.74 +/- 0.15 mN mm<sup>-1</sup>, n = 18, versus PI-diabetic 3.61 +/- 0.19 mN mm<sup>-1</sup>, n = 11, NS; control versus IT-diabetic 4.66 +/- 0.18 mN mm<sup>-1</sup>, n = 22, P < 0.001). 6. Endothelium-dependent relaxation to acetylcholine was

profoundly impaired in the PI-diabetic arteries, but in the IT-diabetic arteries was not significantly different from controls (pEC50: control 7.64 +/- 0.19, n = 17, versus PI-diabetic 6.07 +/- 0.12, n = 8, P < 0.001; control versus IT-diabetic 7.36 +/- 0.09, n = 22, NS). (ABSTRACT TRUNCATED AT 250 WORDS)

L4 ANSWER 226 OF 261 MEDLINE  
AN 94243703 MEDLINE  
DN 94243703 PubMed ID: 7514483  
TI Nitric oxide mediates the stimulation of luteinizing-hormone releasing hormone release induced by glutamic acid in vitro.  
AU Rettori V; Kamat A; McCann S M  
CS Department of Physiology, University of Texas 'Southwestern Medical Center at Dallas 75235-8873.  
NC DK10073 (NIDDK)  
DK43900 (NIDDK)  
SO BRAIN RESEARCH BULLETIN, (1994) 33 (5) 501-3.  
Journal code: B5M; 7605818. ISSN: 0361-9230.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199406  
ED Entered STN: 19940629  
Last Updated on STN: 19960129  
Entered Medline: 19940621  
AB Previous experiments from our laboratory have indicated that LHRH **release is controlled** in vivo and in vitro by NO. Since glutamic acid, the major excitatory transmitter in the brain, has been shown to release LHRH, we wished to determine whether or not this LHRH release was mediated by NO. Consequently, arcuate-median eminence explants from normal male rats were incubated in vitro in Krebs-Ringer bicarbonate glucose (KRBG) media in a Dubnoff metabolic shaker for a preincubation period of 30 min. Fresh media were added containing the substances to be tested and incubation was continued for 30 min. Sodium nitroprusside (NP, 500 microm), which releases NO spontaneously, stimulated the release of LHRH, which indicates that NO can release LHRH. Glutamic acid (10 mM) also produced a robust release of LHRH, and this release was blocked by the inhibitor of NO synthase, NG-monomethyl-L-arginine (NMMA). Furthermore, the release of LHRH induced by glutamic acid was prevented by the addition of hemoglobin (20 micrograms/ml), a scavenger of NO, which would remove the NO released by the action of glutamic acid. The results indicate that glutamic acid stimulated LHRH release is induced by NO.

L4 ANSWER 227 OF 261 MEDLINE  
AN 94194253 MEDLINE  
DN 94194253 PubMed ID: 8145021  
TI Regulation of hepatic endothelial cell and macrophage proliferation and nitric oxide production by GM-CSF, M-CSF, and IL-1 beta following acute endotoxemia.  
AU Feder L S; Laskin D L  
CS Department of Pharmacology and Toxicology, Rutgers University, Piscataway, New Jersey 08855-0789.  
NC ESO5022 (NIEHS)  
GM34310 (NIGMS)  
SO JOURNAL OF LEUKOCYTE BIOLOGY, (1994 Apr) 55 (4) 507-13.  
Journal code: IWY; 8405628. ISSN: 0741-5400.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199405  
ED Entered STN: 19940511  
Last Updated on STN: 19960129

Entered Medline: 19940505

AB Treatment of rats with bacterially derived lipopolysaccharide (LPS), a condition that mimics acute endotoxemia, results in a significant increase in the number of endothelial cells and macrophages in the liver. This is correlated with the release of proinflammatory and cytotoxic mediators that induce liver damage. In the present studies, we analyzed the effects of various inflammatory mediators released during the pathogenesis of hepatic injury on proliferation of liver nonparenchymal cells. To induce acute endotoxemia female Sprague-Dawley rats were injected intravenously with 5 mg/kg LPS. Endothelial cells and macrophages were isolated 48 h later by combined collagenase and pronase perfusion of the liver followed by centrifugal elutriation. Interleukin-1 alpha (IL-1 alpha), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-alpha) had no effect on proliferation of either endothelial cells or macrophages. In contrast, whereas interleukin-1 beta (IL-1 beta) inhibited the proliferation of endothelial cells from untreated rats, this cytokine stimulated the growth of cells from endotoxemic rats. The colony-stimulating factors, granulocyte-macrophage colony-stimulating factor (GM-CSF) and macrophage colony-stimulating factor (M-CSF), also markedly enhanced the proliferation of endothelial cells, as well as macrophages from endotoxemic rats. Macrophages from endotoxemic rats were more sensitive to the colony-stimulating factors than cells from untreated rats. In contrast, the inflammatory mediators LPS and interferon-gamma (IFN-gamma) inhibited endothelial cell and macrophage growth, an effect that was partially blocked in endothelial cells by the nitric oxide synthase inhibitor NG-monomethyl-L-arginine (L-NMMA). This suggests that growth inhibition in these cells is mediated, in part, by nitric oxide. Interestingly, in both endothelial cells and macrophages from endotoxemic rats, GM-CSF, M-CSF, and IL-1 beta synergized with LPS and IFN-gamma to induce nitric oxide production. This was correlated with a further inhibition of proliferation that was partially reversed by L-NMMA in endothelial cells but not macrophages. Taken together these data demonstrate that endothelial cell and macrophage proliferation in the liver is **controlled** by a variety of mediators **released** during endotoxemia; however, the mechanisms regulating growth in the two cell types are distinct.

L4 ANSWER 228 OF 261 MEDLINE

AN 94079912 MEDLINE

DN 94079912 PubMed ID: 8257710

TI Endocytosis and degradation of bovine apo- and holo-lactoferrin by isolated rat hepatocytes are mediated by recycling calcium-dependent binding sites.

AU McAbee D D; Nowatzke W; Oehler C; Sitaram M; Sbaschnig E; Opferman J T; Carr J; Esbensen K

CS Department of Biological Sciences, University of Notre Dame, Indiana 46556.

SO BIOCHEMISTRY, (1993 Dec 14) 32 (49) 13749-60.

Journal code: A0G; 0370623. ISSN: 0006-2960.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199401

ED Entered STN: 19940203

Last Updated on STN: 19970203

Entered Medline: 19940119

AB We characterized endocytosis of iron-saturated (holo) and iron-depleted (apo) 125I-labeled bovine lactoferrin (Lf) by isolated rat hepatocytes. Hepatocytes ingested both Lf forms--determined by EGTA/dextran sulfate removal of surface-bound Lf--at maximal endocytic rates of 1.85 and 1.52 fmol cell<sup>-1</sup> min<sup>-1</sup> for 125I-apo-Lf and 125I-holo-Lf, respectively. First-order endocytic rate constants (37 degrees C) for 125I-apo-Lf and 125I-holo-Lf were 0.276 and 0.292 min<sup>-1</sup>, respectively. Regardless of Lf's

iron content, hyperosmotic media (approximately 500 mmol/kg) inhibited Lf uptake by approximately 90%, indicating endocytosis of both Lf forms was primarily clathrin-dependent. Endocytosis of both Lf forms was not altered significantly in the presence of excess iron chelator desferrioxamine or rat holo-transferrin, or by cycloheximide treatment. Fluorescein isothiocyanate- and cyclohexanedione-modified Lf competed fully with native Lf for binding and endocytosis, indicating that, unlike human Lf, modification of lysine or arginine residues does not block the interaction of bovine Lf with cells. After binding Lf at 4 degrees C, cells at 37 degrees C internalized approximately 90% of Lf bound to Ca(2+)-dependent sites but not Lf bound to Ca(2+)-independent sites. Following uptake, hepatocytes released acid-soluble (degraded) products of 125I-Lf biphasically at 37 degrees C, an initial rapid phase within the first 20 min--more pronounced with 125I-holo-Lf--followed by a **sustained** linear **release** of 298 and 355 molecule equiv cell-1 min-1 for 125I-apo-Lf and 125I-holo-Lf, respectively. At 4 degrees C, both digitonin-permeabilized and intact cells bound approximately  $1.1 \times 10^6$  125I-Lf molecules to Ca(2+)-dependent sites per cell, indicating that hepatocytes do not contain a sizeable intracellular pool of these sites. Moreover, cells retained > 70% of Ca(2+)-dependent sites on the surface during sustained Lf endocytosis. Thus, these Lf binding sites recycle during endocytosis at an estimated 4-5 min/circuit.

L4 ANSWER 229 OF 261 MEDLINE  
 AN 93164523 MEDLINE  
 DN 93164523 PubMed ID: 1287271  
 TI Involvement of nitric oxide in endothelium-dependent, phasic relaxation caused by histamine in monkey cerebral arteries.  
 AU Ayajiki K; Okamura T; Toda N  
 CS Department of Pharmacology, Shiga University of Medical Sciences, Ohtsu, Japan.  
 SO JAPANESE JOURNAL OF PHARMACOLOGY, (1992 Dec) 60 (4) 357-62.  
 Journal code: KO7; 2983305R. ISSN: 0021-5198.  
 CY Japan  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199303  
 ED Entered STN: 19930402  
 Last Updated on STN: 19970203  
 Entered Medline: 19930317  
 AB Monkey cerebral artery strips partially contracted with prostaglandin F2 alpha responded to histamine with biphasic patterns of relaxation. The delayed and sustained relaxation was suppressed by cimetidine, whereas the phasic response was abolished by treatment with chlorpheniramine and NG-nitro-L-arginine (L-NA), a nitric oxide (NO) synthase inhibitor. The inhibition by L-NA was reversed by L-arginine. D-NA was without effect. Endothelium denudation abolished the phasic relaxation. We hypothesized that endothelium-dependent, phasic relaxations caused by histamine are mediated by NO that is **released** by H1-receptor stimulation, whereas the **sustained** relaxation is associated with the activation of H2-receptors in the smooth muscle of monkey cerebral arteries.

L4 ANSWER 230 OF 261 MEDLINE  
 AN 93060391 MEDLINE  
 DN 93060391 PubMed ID: 1434097  
 TI Nitroarginine-sensitive and -insensitive components of the endothelium-dependent relaxation in the guinea-pig carotid artery.  
 AU Suzuki H; Chen G; Yamamoto Y; Miwa K  
 CS Department of Physiology, Nagoya City University Medical School, Japan.  
 SO JAPANESE JOURNAL OF PHYSIOLOGY, (1992) 42 (2) 335-47.  
 Journal code: KON; 2985184R. ISSN: 0021-521X.  
 CY Japan

DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199212  
ED Entered STN: 19930122

Last Updated on STN: 19970203

Entered Medline: 19921203

AB In the guinea-pig carotid arteries, nitroarginine elevated the resting tension (greater than  $3 \times 10^{-6}$  M) and enhanced the noradrenaline (NA)- and high-potassium (high-K, 29.6 mM) induced contractions (greater than  $10^{-7}$  M), in a concentration-dependent manner, with no significant change in the resting membrane potential and depolarizations elicited by NA or high-K. ACh ( $10^{-6}$  M) relaxed the muscles precontracted with NA or high-K by 96 or 46% of the contraction, respectively. In the presence of nitroarginine ( $10^{-5}$  M) for 1-3 h, the ACh-induced relaxation was reduced to 40 or 0% of the NA- or high-K-contractions, respectively. In tissues contracted with NA and exposed to nitroarginine, the ACh-induced relaxation changed from a sustained to a transient form. ACh relaxed the muscles to a similar extent, at any given level of tension, as elevated by different concentrations of NA to 1-3 times the level produced by  $10^{-6}$  M NA, either in the presence or absence of nitroarginine. ACh (greater than  $10^{-8}$  M) produced a transient hyperpolarization of the membrane, in an endothelium-dependent manner, and the responses were blocked by atropine ( $10^{-6}$  M) or high-K solution, but not by NA or nitroarginine. We propose that 1) endothelium-derived hyperpolarizing factor (EDHF) is produced by pathways independent of the biosynthesis of endothelium-derived relaxing factor (EDRF), 2) the **sustained release** of EDRF maintains the muscle tone at a low level, and 3) the endothelium-dependent relaxation is produced by both EDRF and EDHF, and they elicit sustained and transient relaxations, respectively.

L4 ANSWER 231 OF 261 MEDLINE

AN 92384880 MEDLINE

DN 92384880 PubMed ID: 1515019

TI Stimulation of insulin release by vasopressin in the clonal beta-cell line, HIT-T15: the role of protein kinase C.

AU Hughes S J; Carpinelli A; Niki I; Nicks J L; Ashcroft S J

CS Nuffield Department of Clinical Biochemistry, John Radcliffe Hospital, Headington, Oxford, U.K.

SO JOURNAL OF MOLECULAR ENDOCRINOLOGY, (1992 Apr) 8 (2) 145-53.

Journal code: AEG; 8902617. ISSN: 0952-5041.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199210

ED Entered STN: 19921023

Last Updated on STN: 19921023

Entered Medline: 19921007

AB We have studied the effects of vasopressin and tetradecanoyl phorbol acetate (TPA) on cytosolic free  $\text{Ca}^{2+}$  ( $[\text{Ca}^{2+}]_i$ ) and insulin release in HIT-T15 beta-cells. Saturable binding of  $[^3\text{H}]$   $[\text{Arg}^8]$ -vasopressin to HIT cell microsomes indicated a single class of receptors with a dissociation constant ( $K_d$ ) of 2.5 nM and a total number of binding sites ( $B_{\text{max}}$ ) equal to 120 fmol/mg protein.  $[\text{Arg}^8]$ -vasopressin (0.1-100 nM) elicited dose-dependent insulin release from HIT cells by up to 25-fold. This increase was dependent on the presence of extracellular glucose and was blocked by omission of extracellular  $\text{Ca}^{2+}$  or addition of verapamil. The stimulation was biphasic; a rapid but short-lived large increase in **release** was followed by a smaller **sustained** rise. Vasopressin also evoked a marked, concentration-dependent increase in  $[\text{Ca}^{2+}]_i$  which was also biphasic; an initial spike was followed by a sustained elevation. This increase also required glucose and was blocked by the absence of extracellular  $\text{Ca}^{2+}$  or the addition of verapamil.

Pretreatment of the cells with TPA overnight to deplete protein kinase C activity did not affect the  $[Ca^{2+}]_i$  or insulin responses to vasopressin. However, short-term exposure to TPA markedly reduced glucose-induced steady-state  $[Ca^{2+}]_i$ , despite potentiating glucose-stimulated insulin release sevenfold, and blocked the  $[Ca^{2+}]_i$  increase induced by vasopressin. These inhibitory effects of TPA were absent in protein kinase C-depleted cells and were prevented by staurosporine. TPA had no significant effect on vasopressin-induced insulin release. Vasopressin did not modify the activity of ATP-sensitive  $K^+$  channels. (ABSTRACT TRUNCATED AT 250 WORDS)

L4 ANSWER 232 OF 261 MEDLINE

AN 92216787 MEDLINE

DN 92216787 PubMed ID: 1373103

TI Different patterns of release of endothelium-derived relaxing factor and prostacyclin.

AU Mitchell J A; de Nucci G; Warner T D; Vane J R

CS William Harvey Research Institute, Saint Bartholomew's Hospital Medical College, London.

SO BRITISH JOURNAL OF PHARMACOLOGY, (1992 Feb) 105 (2) 485-9.

Journal code: B00; 7502536. ISSN: 0007-1188.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199205

ED Entered STN: 19920529

Last Updated on STN: 19960129

Entered Medline: 19920508

AB 1. Release of endothelium derived relaxing factor (EDRF) and prostacyclin (PGI<sub>2</sub>) from endothelial cells (EC) cultured from bovine aortae was measured by bioassay and radioimmunoassay, respectively, during infusions (10 min) of bradykinin (BK), adenosine diphosphate (ADP), arachidonic acid (AA), alkaline buffers and the free-bases (FB) of L-arginine or D-arginine. Release of EDRF from the luminally perfused rabbit aorta was also measured during infusions (10 min) of acetylcholine (ACh), substance P and ADP. 2. Bradykinin (10 or 30 nM) infused through the column of EC induced release of both EDRF and PGI<sub>2</sub>, neither of which was maintained for the duration of the infusion. 3. ADP (1.6 or 4 microM) infused through the column of EC induced release of a EDRF which was maintained for the duration of the infusion and a release of PGI<sub>2</sub> which lasted for a much shorter period. 4. Arachidonic acid (30 or 90 microM) infused through the column of EC caused a **sustained release** of EDRF and PGI<sub>2</sub>, both of which outlasted the infusion of AA. 5. L-Arginine FB, D-arginine FB or alkaline buffer infused through the column of EC released EDRF, but only small amounts of PGI<sub>2</sub>. The release of EDRF outlasted the period of infusion and was due to an increase in the pH of the Krebs solution perfusing the EC. 6. Infusions of ACh (0.25-1 microM) or ADP (4-16 microM) caused a **sustained release** of EDRF from the luminally-perfused rabbit aorta, whereas infusion of substance P (3.3-10 microM) caused only a transient release of EDRF. 7. These results show that distinct patterns of EDRF release exist to different agonists in both cultured and in situ EC, and that EDRF and PGI<sub>2</sub> do not necessarily follow the same time course of **release**. Furthermore, **sustained release** of EDRF does not require the constant infusion of the precursor, L-arginine, whereas **sustained release** of PGI<sub>2</sub> only occurs when AA, the precursor of PGI<sub>2</sub>, is present in the extracellular medium.

L4 ANSWER 233 OF 261 MEDLINE

AN 91292649 MEDLINE

DN 91292649 PubMed ID: 1712259

TI Stimulus-secretion coupling of arginine-induced insulin release: significance of changes in extracellular and intracellular pH.

AU Malaisse W J; Plasman P O; Blachier F; Herchuelz A; Sener A  
 CS Laboratory Experimental Medicine, Brussels Free University, Belgium.  
 SO CELL BIOCHEMISTRY AND FUNCTION, (1991 Jan) 9 (1) 1-7.  
 Journal code: C9W; 8305874. ISSN: 0263-6484.  
 CY ENGLAND: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199108  
 ED Entered STN: 19910901  
 Last Updated on STN: 19970203  
 Entered Medline: 19910809

AB The possible relevance of changes in extracellular and/or intracellular pH to the insulinotropic action of L-arginine and L-homoarginine was investigated in rat pancreatic islets. A rise in extracellular pH from 7.0 to 7.4 and 7.8 augmented the secretory response to these cationic amino acids whilst failing to affect the uptake of L-arginine by islet cells and whilst decreasing the release of insulin evoked by D-glucose. Under these conditions, a qualified dissociation was also observed between secretory data and <sup>45</sup>Ca net uptake. Moreover, at high extracellular pH, the homoarginine-induced increase in <sup>86</sup>Rb outflow from prelabelled islets rapidly faded out, despite **sustained** stimulation of insulin **release**. The cationic amino acids failed to affect the intracellular pH of islet cells, whether in the absence or presence of D-glucose and whether at normal or abnormal extracellular pH. These findings argue against the view that the secretory response to L-arginine would be related to either a change in cytosolic pH or the accumulation of this positively charged amino acid in the beta-cell. Nevertheless, they suggest that the yet unidentified target for L-arginine and its non-metabolized analogue in islet cells displays pH-dependency with optimal responsiveness at alkaline pH.

L4 ANSWER 234 OF 261 MEDLINE  
 AN 91031733 MEDLINE  
 DN 91031733 PubMed ID: 2226624  
 TI Cultured endothelial cells maintain their L-arginine level despite the continuous release of EDRF.

AU Mitchell J A; Hecker M; Anggard E E; Vane J R  
 CS William Harvey Research Institute, St. Bartholomew's Hospital Medical College, London, U.K.  
 SO EUROPEAN JOURNAL OF PHARMACOLOGY, (1990 Jul 17) 182 (3) 573-6.  
 Journal code: EN6; 1254354. ISSN: 0014-2999.  
 CY Netherlands  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199012  
 ED Entered STN: 19910208  
 Last Updated on STN: 19910208  
 Entered Medline: 19901212

AB Endothelial cells cultured from bovine aorta and grown on microcarrier beads contain 107 +/- 9 microM L-arginine (Arg; n = 11). When packed into a jacketed chromatography column and perfused with Krebs solution, the cells showed a substantial and **sustained release** of endothelium-derived relaxing factor (EDRF) for up to 2 h, which was further enhanced by infusions of adenosine diphosphate (4 microM). In contrast to other amino acids, such as L-alanine, L-aspartate, L-glutamine, L-glutamate or L-serine, which showed a time-dependent decrease to less than 30% of their original level within 2 h, Arg remained at control levels for 30 min and decreased only by 25% after 2 h. Thus endothelial cells can generate Arg from an intracellular source to maintain their Arg level despite the continuous formation of EDRF.

L4 ANSWER 235 OF 261 MEDLINE

AN 90298841 MEDLINE  
 DN 90298841 PubMed ID: 2113861  
 TI Stimulus-secretion coupling of arginine-induced insulin release: comparison with histidine-induced insulin release.  
 AU Sener A; Blachier F; Rasschaert J; Malaisse W J  
 CS Laboratory of Experimental Medicine, Brussels Free University, Belgium.  
 SO ENDOCRINOLOGY, (1990 Jul) 127 (1) 107-13.  
 Journal code: EGZ; 0375040. ISSN: 0013-7227.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 199008  
 ED Entered STN: 19900907  
 Last Updated on STN: 19970203  
 Entered Medline: 19900808  
 AB L-Histidine, when tested at a 10-mM concentration, caused a rapid and **sustained** stimulation of insulin **release** from rat islets exposed to either D-glucose (7.0 or 8.3 mM) or L-leucine (10.0 mM). The stimulation of insulin release could not be ascribed to an increase in oxygen uptake, to the generation of histamine from L-histidine, or to its participation in a transglutaminase-catalyzed reaction. Like other cationic amino acids, however, L-histidine rapidly accumulated in islet cells, increased 86Rb outflow from prelabeled islets perfused in the presence or absence of extracellular Ca<sup>2+</sup>, and stimulated the entry of Ca<sup>2+</sup> into islet cells. Yet, the amount of exogenous L-histidine present in the islet cells with a positively charged side chain was estimated to be below the threshold value required for stimulation of insulin release by fully ionized cationic amino acids, such as L-arginine. Hence, the present findings argue against the view that the insulinotropic action of cationic amino acids is solely attributable to the accumulation of these positively charged molecules inside the islet B cell with subsequent depolarization of the plasma membrane.

L4 ANSWER 236 OF 261 MEDLINE  
 AN 85126677 MEDLINE  
 DN 85126677 PubMed ID: 2857640  
 TI Multiple effects of leucine on glucagon, insulin, and somatostatin secretion from the perfused rat pancreas.  
 AU Leclercq-Meyer V; Marchand J; Woussen-Colle M C; Giroix M H; Malaisse W J  
 SO ENDOCRINOLOGY, (1985 Mar) 116 (3) 1168-74.  
 Journal code: EGZ; 0375040. ISSN: 0013-7227.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 198503  
 ED Entered STN: 19900320  
 Last Updated on STN: 19980206  
 Entered Medline: 19850327  
 AB The effects of increasing concentrations of leucine (0.2, 2.0, and 15.0 mmol/liter) on glucagon secretion from the perfused rat pancreas were examined at various glucose levels (0, 3.3, or 8.3 mmol/liter) and in the absence or presence of either arginine (5.0 mmol/liter) or glutamine (10.0 mmol/liter). At a low glucose concentration (3.3 mmol/liter), leucine caused a dose-related biphasic increase in glucagon output in the absence of arginine, but only a transient increase in the presence of the latter amino acid. These positive responses were markedly reduced and, on occasion, abolished at a high glucose concentration (8.3 mmol/liter). Moreover, at a low glucose concentration (3.3 mmol/liter) and in the presence of arginine, the highest concentration of leucine (15.0 mmol/liter) provoked a **sustained** and reversible inhibition of glucagon **release**. Likewise, leucine (15.0 mmol/liter) reversibly inhibited glucagon secretion evoked by glutamine in the absence of

glucose. Thus, leucine exerted a dual effect on the secretion of glucagon, the inhibitory effect of leucine prevailing at a high concentration of the branched chain amino acid and when glucagon secretion was already stimulated by arginine or glutamine. At a physiological concentration (0.2 mmol/liter), however, leucine was a positive stimulus for glucagon release, especially in the absence of another amino acid. Concomitantly, leucine was always a positive stimulus for both insulin and somatostatin secretion. The intimate mechanisms involved in the dual effect of leucine on glucagon secretion remain to be elucidated.

L4 ANSWER 237 OF 261 MEDLINE

AN 84220011 MEDLINE

DN 84220011 PubMed ID: 6374488

TI Depending on the stimulus, central serotonergic activation by fenfluramine blocks or does not alter growth hormone secretion in man.

AU Casanueva F F; Villanueva L; Penalva A; Cabezas-Cerrato J

SO NEUROENDOCRINOLOGY, (1984 Apr) 38 (4) 302-8.

Journal code: NY8; 0035665. ISSN: 0028-3835.

CY Switzerland

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198407

ED Entered STN: 19900320

Last Updated on STN: 19900320

Entered Medline: 19840702

AB The role of serotonin (5-HT) in the hypothalamic regulation of human growth hormone (GH) was reassessed through the use of fenfluramine, which selectively releases 5-HT from presynaptic terminals. Oral administration of L-dopa plus propranolol induced a potent and **sustained GH release** in the subjects tested (26 +/- 6 ng/ml). The administration of fenfluramine (20 mg i.v. as bolus plus 20 mg/30 min i.v.) completely suppressed the L-dopa-induced GH secretion (2 +/- 0.5 ng/ml). On the other hand, when arginine (30 g/30 min i.v.) was used as a GH stimulant of medium intensity (12.7 +/- 2.8 ng/ml), fenfluramine at the same dose was not able to alter the pattern of pituitary secretion (11.5 +/- 4.2 ng/ml). Fenfluramine alone induced a slight nonsignificant decrease in GH values with a parallel and significant increase in prolactin (PRL) secretion in accordance with the proposed serotonergic activity of the drug. Rat PRL secretion by pituitaries incubated in vitro was inhibited by dopamine. Fenfluramine added to the system did not counteract the dopaminergic reduction of PRL release, making unlikely the possibility of an antagonism at the dopaminergic receptor as mechanism of action of fenfluramine on PRL secretion. In conclusion, depending on the stimulus under study, serotonergic activation by fenfluramine either inhibits or does not alter GH secretion in man. No proof of a serotonergic stimulatory component on GH regulation has been detected in this study. Fenfluramine is a valuable tool in neuroendocrinological studies, dealing with serotonergic mechanisms.

L4 ANSWER 238 OF 261 MEDLINE

AN 82116856 MEDLINE

DN 82116856 PubMed ID: 6120069

TI Effects of K+ and arginine on insulin, glucagon, and somatostatin release from the in vitro perfused rat pancreas.

AU Frankel B J; Heldt A M; Grodsky G M

NC AM-01410 (NIADDK)

AM-26033 (NIADDK)

SO ENDOCRINOLOGY, (1982 Feb) 110 (2) 428-31.

Journal code: EGZ; 0375040. ISSN: 0013-7227.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 198204  
ED Entered STN: 19900317  
Last Updated on STN: 19970203  
Entered Medline: 19820412  
AB Rat pancreases were perfused in vitro for 5-min periods with K<sup>+</sup> alone (8, 10, and 12 mM) or in the presence of arginine (10 mM). Alone, K<sup>+</sup> caused bursts of insulin, glucagon, and somatostatin (SRIF) release; with arginine, it caused a burst of insulin and **sustained** SRIF **release**, but caused **sustained** suppression of glucagon. This suppression correlated better with SRIF than insulin release. Therefore, if a paracrine effect is responsible for the inhibition of glucagon secretion under these circumstances, SRIF is a more likely candidate than insulin.

L4 ANSWER 239 OF 261 MEDLINE  
AN 80151153 MEDLINE  
DN 80151153 PubMed ID: 7361908  
TI Adenosine **release** during early and **sustained** exercise of canine skeletal muscle.  
AU Tominaga S; Curnish R R; Belardinelli L; Rubio R; Berne R M  
SO AMERICAN JOURNAL OF PHYSIOLOGY, (1980 Feb) 238 (2) H156-63.  
Journal code: 3U8; 0370511. ISSN: 0002-9513.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 198005  
ED Entered STN: 19900315  
Last Updated on STN: 19900315  
Entered Medline: 19800514  
AB During contraction of skeletal muscle in the isolated dog hindlimb under constant-flow perfusion, the specific activity of infused [8-<sup>14</sup>C]adenosine (nonvasoactive concn) in venous effluents decreased to 7% of the resting level in 1.25 min and was associated with a concomitant decrease in vascular resistance to 39% of the resting value. Since this decrease in specific activity of labeled adenosine could have been due to 1) an enhanced adenosine release by parenchymal tissue, 2) an exercise-induced increase in the number of open capillaries (greater surface area) in the absence of increased adenosine production 3) some degree of tissue hypoxia, or 4) a combination of these factors, experiments with maximally dilated vessels were performed. Acetylcholine and a nonvasoactive concentration of [8-<sup>14</sup>C]adenosine were continuously infused into an isolated dog hindlimb which was perfused at constant flow during periods of rest, contraction, and recovery while arterial oxygenation was maintained at normoxic levels. Approximately 2.75 min after the onset of contraction with the vascular bed maximally dilated, the specific activity of [8-<sup>14</sup>C]adenosine in venous effluents decreased to 38% of the resting level while the venous Po<sub>2</sub> decreased from 78 to 42 mmHg; the value of 42 mmHg indicates apparent absence of hypoxia in the muscle. These observations are consistent with the concept that adenosine release is involved in the vasodilation observed in contraction of skeletal muscle.

L4 ANSWER 240 OF 261 MEDLINE  
AN 77139018 MEDLINE  
DN 77139018 PubMed ID: 849811  
TI Glucagon secretion induced by natural and artificial amino acids in the perfused rat pancreas.  
AU Assan R; Attali J R; Ballerio G; Boillot J; Girard J R  
SO DIABETES, (1977 Apr) 26 (4) 300-7.  
Journal code: E8X; 0372763. ISSN: 0012-1797.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English

FS Abridged Index Medicus Journals; Priority Journals  
 EM 197705  
 ED Entered STN: 19900313  
 Last Updated on STN: 19900313  
 Entered Medline: 19770527

AB The glucagon-secreting potency of 22 amino acids was investigated in the rat isolated perfused pancreas. Arginine and the structurally related amino acids were the most potent A2-cell stimulators that induced a biphasic and **sustained** glucagon release. Dose-response curves were different for L(+) and D(+) arginine, and the suppressor effect of glucose on the response to L(+) arginine was not detected in the presence of D(+) arginine or homoarginine. Citrulline was the only exception among the arginine-related amino acids; it displayed neither stimulatory nor inhibitory potency on glucagon release. The A2-cell response to D(+) amino acids and artificial analogues of arginine is a strong case for the theory of amino acid receptors' triggering the release of the hormone before (or in the absence of) further metabolism. The prominent rank of arginine and ornithine among stimulatory amino acids and some other physiologic evidence suggest that A2-cell may play a regulatory role in the metabolism of ammonia by the liver.

L4 ANSWER 241 OF 261 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 AN 2001:147286 BIOSIS  
 DN PREV200100147286  
 TI Neurohormonal prediction of left ventricular anti-remodeling during beta-blockade with metoprolol in chronic heart failure.  
 AU Groenning, Bjoern A. (1); Nilsson, Jens C. (1); Kjaer, Andreas; Sondergaard, Lars; Fritz-Hansen, Thomas; Larsson, Henrik B. W.; Hildebrandt, Per R.  
 CS (1) Danish Research Ctr of Magnetic Resonance, Copenhagen Denmark  
 SO Circulation, (October 31, 2000) Vol. 102, No. 18 Supplement, pp. II.779. print.  
 Meeting Info.: Abstracts from Scientific Sessions 2000 New Orleans, Louisiana, USA November 12-15, 2000  
 ISSN: 0009-7322.  
 DT Conference  
 LA English  
 SL English

L4 ANSWER 242 OF 261 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 AN 2001:98392 BIOSIS  
 DN PREV200100098392  
 TI Nitric oxide modulation of interleukin-1beta-evoked intracellular Ca2+ release in human astrocytoma U-373 MG cells and brain striatal slices.  
 AU Meini, Antonella; Benocci, Alberto; Frosini, Maria; Sgaragli, Gianpietro; Pessina, Gianpaolo; Aldinucci, Carlo; Youmbi, Gisele Tchuisseu; Palmi, Mitri (1)  
 CS (1) Istituto di Scienze Farmacologiche, Universita di Siena, via Piccolomini 170, 53100, Siena: palmi@unisi.it Italy  
 SO Journal of Neuroscience, (December 15, 2000) Vol. 20, No. 24, pp. 8980-8986. print.  
 ISSN: 0270-6474.  
 DT Article  
 LA English  
 SL English

AB Intracellular Ca2+ mobilization and release into mammal CSF plays a fundamental role in the etiology of fever induced by the proinflammatory cytokine interleukin-1beta (IL-1beta) and other pyrogens. The source and mechanism of IL-1beta-induced intracellular Ca2+ mobilization was investigated using two experimental models. IL-1beta (10 ng/ml) treatment of rat striatal slices preloaded with 45Ca2+ elicited a delayed (30 min) and **sustained** increase (125-150%) in spontaneous 45Ca2+ **release** that was potentiated by L-arginine (300 muM) and counteracted by N-omega-nitro-L-arginine methyl ester

(L-NAME) (1 and 3 mM). The nitric oxide (NO) donors diethylamine/NO complex (sodium salt) (0.3 and 1 mM) and spermine/NO (0.1 and 0.3 mM) mimicked the effect of IL-1beta on Ca<sup>2+</sup> release. IL-1beta stimulated tissue cGMP concentration, and dibutyl cGMP enhanced Ca<sup>2+</sup> release. The guanyl cyclase inhibitors 1 H-(1,2,4)oxadiazole (4,3-a)quinoxalin-1-one (100  $\mu$ M) and 6-(phenylamino)-5,8 quinolinedione (50  $\mu$ M) counteracted Ca<sup>2+</sup> release induced by 2.5 but not 10 ng/ml IL-1beta. Ruthenium red (50  $\mu$ M) and, to a lesser extent, heparin (3 mg/ml) antagonized IL-1beta-induced Ca<sup>2+</sup> release, and both compounds administered together completely abolished this response. Similar results were obtained in human astrocytoma cells in which IL-1beta elicited a delayed (30 min) increase in intracellular Ca<sup>2+</sup> concentration ((Ca<sup>2+</sup>)<sub>i</sub>) (402  $\pm$  71.2% of the baseline), which was abolished by 1 mM L-NAME. These data indicate that the NO/cGMP-signaling pathway is part of the intracellular mechanism transducing IL-1 beta-evoked Ca<sup>2+</sup> mobilization in glial and striatal cells and that the ryanodine and the inositol-(1,4,5)-trisphosphate-sensitive Ca<sup>2+</sup> stores are involved.

- L4 ANSWER 243 OF 261 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 AN 2001:67169 BIOSIS  
 DN PREV200100067169  
 TI Preparation and characterization of acrylic hydrogels neutralized by basic amino acids.  
 AU Uchida, Takahiro (1); Toida, Yuka; Miyanaga, Yohko; Machida, Kotoe; Wada, Koichi; Ohki, Toshimitsu; Matsuyama, Kenji  
 CS (1) School of Pharmaceutical Sciences, Mukogawa Women's University, 11-68, Koshien 9-Bancho, Nishinomiya, 663-8179 Japan  
 SO Chemical & Pharmaceutical Bulletin (Tokyo), (November, 2000) Vol. 48, No. 11, pp. 1828-1830. print.  
 ISSN: 0009-2363.  
 DT Article  
 LA English  
 SL English  
 AB Basic amino acids were used as neutralizers in the gelation of Eudispert(R) as an acrylic hydrogel. Arginine and lysine successfully neutralized Eudispert(R), as did sodium hydroxide, and formed hydrogels. A gentle rise of pH was observed as the dosage of the base increased when arginine and lysine were used, in contrast to the sharp rise of pH observed when sodium hydroxide was used. The rank of viscosity of the prepared hydrogels was as follows: lysine>arginine>NaOH. The release rate of model drugs (salicylic acid, theophylline, and bovine insulin) from the prepared hydrogels ranked as follows: NaOH>lysine>arginine, the **sustained-release** profile being observed with arginine. The rate of diffusion of the model drug from the hydrogel was inversely proportional to the molecular weight of the cationized neutralizer used. It is concluded that the strategy of neutralization of acidic polymers by basic amino acids has advantage with the respect to both the **sustained-release** characteristics of the gel and the biocompatibility of the basic amino acids themselves.
- L4 ANSWER 244 OF 261 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 AN 1999:491117 BIOSIS  
 DN PREV199900491117  
 TI 7-nitroindazole, a selective inhibitor of nNOS, increases hippocampal extracellular glutamate concentration in status epilepticus induced by kainic acid in rats.  
 AU Alabadi, Jose A. (1); Thibault, Jean-Luc; Pinard, Elisabeth; Seylaz, Jacques; Lasbennes, Francois  
 CS (1) Departamento de Fisiologia, Facultad de Farmacia, Universidad de Valencia, Avda. Vicent Andres Estelles s.n., Burjassot, E-46100, Valencia Spain  
 SO Brain Research, (Aug. 28, 1999) Vol. 839, No. 2, pp. 305-312.  
 ISSN: 0006-8993.  
 DT Article

LA English  
 SL English  
 AB The glutamate extracellular concentration is **controlled** by metabolic and neuronal pathways via **release** and uptake mechanisms. Stimulation of glutamate receptors induces neuronal nitric oxide (NO) release, which in turn modulates glutamate transmission. In this study, the influence of neuronally derived NO on hippocampal glutamate extracellular concentration was investigated in conditions of intense metabolic activation, i.e., during status epilepticus induced by systemic kainic acid (KA). Glutamate, arginine and citrulline concentrations were measured by microdialysis coupled to HPLC. Experiments were performed in conscious rats implanted with a microdialysis probe within the hippocampal CA3 area. Three groups were used: (1) rats treated with KA i.p. (12 mg/kg) and vehicle locally, via the microdialysis probe (n = 9); (2) rats given KA i.p. and a selective inhibitor of neuronal NO synthase, 7-nitroindazole (7-NI, 1.25 mM) locally (n = 13); (3) rats treated with saline i.p. and 7-NI locally (n = 7). Infusion of 7-NI or vehicle was performed throughout the second hour of status epilepticus. In groups 1 and 3, no significant modifications of extracellular glutamate, arginine and citrulline concentrations were measured. In group 2, the local application of 7-NI in the hippocampus during status epilepticus significantly increased extracellular glutamate and arginine concentrations, whereas citrulline concentration remained constant. The concomitant increases of extracellular glutamate and arginine concentrations under local 7-NI perfusion in seizure conditions, suggest that glutamate and arginine are linked in a common metabolic pathway and/or that glutamate is involved in the cross-talk between glia and neurons. A cerebrovascular effect of 7-NI which triggers glutamate release may also occur.

L4 ANSWER 245 OF 261 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 AN 1997:176464 BIOSIS  
 DN PREV199799468177  
 TI Effects of L-arginine and N-omega-nitro-L-arginine methyl ester on cardiac perfusion and function after 1-day cold preservation of isolated hearts.  
 AU Stowe, David F. (1); Boban, Mladen; Roerig, David L.; Chang, David; Palmisano, Barbara W.; Bosnjak, Zeljko J.  
 CS (1) 462 Med. Educ. Build., Med. Coll. Wisconsin, Milwaukee Regional Med. Cent., 8701 W. Watertown Plank Rd., Milwaukee, WI 53226 USA  
 SO Circulation, (1997) Vol. 95, No. 6, pp. 1623-1634.  
 ISSN: 0009-7322.  
 DT Article  
 LA English  
 AB Background. Coronary flow responses to endothelium-dependent (acetylcholine (ACh) or 5-hydroxytryptamine (5-HT)) and endothelium-independent (adenosine (ADE) or nitroprusside (NP)) vasodilators may be altered before and after 1-day hypothermia during the perfusion of arginine vasopressin (AVP), D-arginine (D-ARG), L-arginine (L-ARG), or nitro-L-arginine methyl ester (L-NAME). Methods and Results. Four groups of guinea pig hearts (37.5 degree C (warm)) were perfused for 6 hours with AVP, L-ARG, L-NAME, or nothing (control). Five heart groups (cold) were perfused with AVP, D-ARG, L-ARG, L-NAME, or nothing (control), but after 2 hours they were perfused at low flow for 22 hours at 3.7 degree C and again for 3 hours at 37.5 degree C. ADE, butanedione monoxime, and NP were given for cardioprotection before, during, and after hypothermia. In warm groups, L-ARG did not alter basal flow or ADE, ACh, 5-HT, or NP responses, whereas L-NAME and AVP reduced basal flow and the ADE response, abolished ACh and 5-HT responses, and increased the NP response. In cold groups after hypothermia, L-ARG did not alter basal flow, but L-NAME, AVP, D-ARG, and control reduced flow. In the postcold L-ARG group, ACh increased peak flow, but NP did not increase flow in other cold groups. Effluent L-ARG and L-CIT in the cold control group fell from 64+-9 and 9+-1 mu-g/L at 1 hour to 36+-5 and 5+-1 mu-g/L at 25 hours, respectively. Left ventricular pressure and cardiac efficiency improved

more in the postcold L-ARG group than in the postcold D-ARG, AVP, and L-NAME groups. Conclusions. Endogenous effluent levels of L-ARG and L-CIT decrease after 24 hours in isolated hearts, whereas perfusion of L-ARG improves cardiac performance, basal coronary flow, and vasodilator responses. In contrast, L-NAME, L-ARG, and AVP limit flow and performance but maintain a partial vasodilatory response to NP. **Sustained release** of NO may account for improved performance after L-ARG after hypothermia.

L4 ANSWER 246 OF 261 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
AN 1997:170081 BIOSIS  
DN PREV199799476684  
TI Microencapsulation of rh-erythropoietin, using biodegradable poly(D,L-lactide-co-glycolide): Protein stability and the effects of stabilizing excipients.  
AU Morlock, Michael; Koll, Hans; Winter, Gerhard; Kissel, Thomas (1)  
CS (1) Dep. Pharmaceuticals Biopharm., Philipps Univ., Ketzertbach 63, D-35032 Marburg Germany  
SO European Journal of Pharmaceutics and Biopharmaceutics, (1997) Vol. 43, No. 1, pp. 29-36.  
ISSN: 0939-6411.  
DT Article  
LA English  
AB Parenteral delivery systems allowing **controlled drug release** over one month are of particular interest for proteins and peptides. We investigated the microencapsulation of recombinant human erythropoietin (EPO), a stimulating factor of red blood cell production, into poly(D,L-lactide-co-glycolide) (PLG) microspheres, using a water-in-oil-in-water (W/O/W) double emulsion technique. The integrity and stability of EPO during microencapsulation and storage was characterized. Effects of various excipients on in vitro release properties and formation of EPO aggregates were investigated. The formation of EPO aggregates in the W/O/W double emulsion technique was mainly influenced by the first homogenizing step, when preparing the water-in-oil (W/O) emulsion, whereas the subsequent processing steps, including drying, proved to be noncritical. A rotor/stator homogenizer generated ca. 5% covalently bound EPO aggregates, ultrasonication and vortexing slightly increased aggregate-formation, as demonstrated by size-exclusion chromatography and native-polyacrylamide gel electrophoresis (PAGE). Using excipients, such as hydroxypropyl-beta-cyclodextrin, L-arginine, or bovine serum albumin (BSA), a distinct reduction of the formation of EPO aggregates could be achieved. The discontinuous in vitro release behavior from PLG microspheres was not significantly modified by these additives, influencing predominantly the initial drug release phase. During the in vitro release, an accumulation of EPO aggregates in the residual microparticles was detected, which could not be suppressed by excipients. An accelerated stability test demonstrated no change in drug content, release behavior and aggregate profile over 56 days at -20, 8 degree C or room temperature.

L4 ANSWER 247 OF 261 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
AN 1995:502467 BIOSIS  
DN PREV199598526017  
TI Nitric oxide controls arteriolar tone in the retina of the miniature pig.  
AU Donati, G.; Pournaras, C. J. (1); Munoz, J.-L.; Poitry, S.; Poitry-Yamate, C. L.; Tsacopoulos, M.  
CS (1) Univ. Hosp. Eye Clinic, Rue Alcide-Jentzer 22, CH-1211 Geneva 4 Switzerland  
SO Investigative Ophthalmology & Visual Science, (1995) Vol. 36, No. 11, pp. 2228-2237.  
ISSN: 0146-0404.  
DT Article  
LA English  
AB Purpose: Experimental evidence indicates that the retinal microcirculation

is mainly controlled by factors released from the tissue surrounding the arterioles. This study explores whether nitric oxide (NO), a possible factor, is released in the retina and controls the arteriolar tone. Methods: Using a NO microprobe, the authors measured (NO) in the preretinal vitreous of miniature pigs as a function of distance from the retinal surface. Additionally, the NO-synthase inhibitor nitro-L-arginine was pressure injected. Finally, the retinal pool size of arginine and its biosynthesis from  $^{14}\text{C}(\text{U})$ -glucose were biochemically assessed on retinal tissue and acutely isolated Muller cells. Results: At the retinal surface, (NO) measured 6 to 9  $\mu\text{M}$ , and, in the vitreous, it fell to zero approximately 180  $\mu\text{m}$  away from the retina. Therefore, NO is degraded faster in the vitreous (65 to 80  $\mu\text{M}$   $\text{cntdot}$   $\text{minute}^{-1}$ ) than in aqueous solution. Light flicker stimulation of the dark-adapted retina induced a reversible increase of (NO) (  $\text{apprxeq}$  1.6  $\mu\text{M}$ ). Preretinal juxta-arteriolar microinjections of nitro-L-arginine (0.6 mM) induced a segmental and reversible arteriolar vasoconstriction of 45%; in contrast, intravenous infusion of nitro-L-arginine had no measurable effect on arteriolar diameter. The retinal pool size of arginine was small (  $\text{ltoreq}$  200  $\mu\text{M}$ ), but there was an important rate of arginine biosynthesis in Muller cells. Conclusions: These results strongly suggest that cells in the retina, other than endothelial cells, produce and release NO, which in turn controls the basal dilating arteriolar tone in the inner retina.

\* \* \* \* \* STN Columbus \* \* \* \* \*

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Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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worldwide, or send an e-mail to [help@cas.org](mailto:help@cas.org) for further assistance or to  
receive a credit for any duplicate searches.

=> e arginine/cn

E1	1	ARGININANILIDE, N.ALPHA.,N.OMEGA.,N.OMEGA.-TRIS(PHENYLCARBAM OYL)-, L-/CN
E2	1	ARGININANILIDE, N2-BENZOYL-/CN
E3	2 -->	ARGININE/CN
E4	1	ARGININE .BETA.-NAPHTHYLAMIDE/CN
E5	1	ARGININE 2,2,2-TRICHLOROETHYL ESTER/CN
E6	1	ARGININE 2-MONOOXYGENASE/CN
E7	1	ARGININE 3RD TRANSPORT SYSTEM PERIPLASMIC BINDING PROTEIN (E SCHERICHIA COLI O157:H7 STRAIN EDL933 GENE ARTI)/CN
E8	1	ARGININE 3RD TRANSPORT SYSTEM PERIPLASMIC BINDING PROTEIN (E SCHERICHIA COLI O157:H7 STRAIN EDL933 GENE ARTJ)/CN
E9	1	ARGININE 3RD TRANSPORT SYSTEM PERIPLASMIC BINDING PROTEIN (E SCHERICHIA COLI STRAIN O157:H7 GENE ECS0943)/CN
E10	1	ARGININE 3RD TRANSPORT SYSTEM PERIPLASMIC BINDING PROTEIN (E SCHERICHIA COLI STRAIN O157:H7 GENE ECS0946)/CN
E11	1	ARGININE 3RD TRANSPORT SYSTEM PERMEASE PROTEIN (ESCHERICHIA

COLI 0157:H7 STRAIN EDL933 GENE ARTM)/CN  
E12 1 ARGININE 3RD TRANSPORT SYSTEM PERMEASE PROTEIN (ESCHERICHIA  
COLI 0157:H7 STRAIN EDL933 GENE ARTQ)/CN

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L1 2 ARGININE/CN

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L4 261 L2 AND L3

=> s nitric oxid## or NO

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L5 7452226 NITRIC OXID## OR NO

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L6 82 L5 AND L4

=> s endothelium

L7 222939 ENDOTHELIUM

=> s l7 and l4

L8 49 L7 AND L4

=> s l6 and l8

L9 41 L6 AND L8

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L10 38 DUP REMOVE L9 (3 DUPLICATES REMOVED)

=> d l10 1-38 bib,ab

L10 ANSWER 1 OF 38 USPATFULL

AN 2002:31986 USPATFULL

TI Compositions and methods for improving vascular health

IN Schmitz, Harold H., Branchburg, NJ, UNITED STATES

Chevaux, Kati A., Seattle, WA, UNITED STATES

Dombroski, Amy, Stanhope, NJ, UNITED STATES

Jerome, Ralph, Blairstown, NJ, UNITED STATES

PI US 2002018807 A1 20020214

AI US 2001-829782 A1 20010410 (9)

PRAI US 2000-197135P 20000414 (60)

DT Utility

FS APPLICATION

LREP Clifford Chance Rogers & Wells LLP, 200 Park Avenue, New York, NY,  
10166-0153

CLMN Number of Claims: 43

ECL Exemplary Claim: 1

DRWN 8 Drawing Page(s)

LN.CNT 1579

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to compositions containing polyphenols, for example, cocoa polyphenols such as procyanidins, in combination with at least one cholesterol lowering agent, and methods for improving vascular health including treating and preventing atherosclerosis and cardiovascular disease.

L10 ANSWER 2 OF 38 USPATFULL

AN 2001:237988 USPATFULL

TI Use of **nitric oxide** scavengers to treat side effects caused by therapeutic administration of sources of **nitric oxide**

IN Lai, Ching-San, Encinitas, CA, United States

PI US 2001056108 A1 20011227

AI US 2001-912757 A1 20010724 (9)

RLI Division of Ser. No. US 1998-103640, filed on 23 Jun 1998, GRANTED, Pat. No. US 6265420

DT Utility

FS APPLICATION

LREP Kevin J. Forrestal, FOLEY & LARDNER, 23rd Floor, 402 West Broadway, San Diego, CA, 92101-3542

CLMN Number of Claims: 56

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 1083

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB **Nitric oxide** scavengers, such as dithiocarbamate-containing compounds, are used to reduce side effects caused by therapeutic administration of **nitric oxide** sources by administering the **nitric oxide** scavenger(s) to the subject after the therapeutic effect of the **nitric oxide** source has been achieved. For example, the **nitric oxide** source can be coadministered with the **nitric oxide** scavenger, with the latter formulated in a time release vehicle selected to delay release of the scavenger for a period of time sufficient to ensure that the therapeutic goal of the **nitric oxide** source has been achieved before release of the scavenger. Formulations and kits, including a bubble pack with pairwise arrangement of unit doses of a desired

**nitric oxide** source and **nitric oxide** scavenger, are also provided. The side effects of sildenafil citrate (Viagra.RTM.), or of simultaneous administration of such a **nitric oxide** source in combination with another, such as nitroglycerin, are effectively controlled by the methods, formulations and kits of the invention.

L10 ANSWER 3 OF 38 USPATFULL

AN 2001:237948 USPATFULL

TI METHOD OF TREATMENT AND PREVENTION OF **NITRIC OXIDE**

DEFICIENCY-RELATED DISORDERS WITH CITRULLINE AND CITRULLINE DERIVATIVES

IN CHWALISZ, KRISTOF, BERLIN, Germany, Federal Republic of

GARFIELD, ROBERT E., FRIENDSWOOD, TX, United States

SHI, SHAO-QUING, GALVESTON, TX, United States

PI US 2001056068 A1 20011227

AI US 1998-34351 A1 19980304 (9)

DT Utility

FS APPLICATION

LREP MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE

1400, ARLINGTON, VA, 22201

CLMN Number of Claims: 28

ECL Exemplary Claim: 1

DRWN 3 Drawing Page(s)

LN.CNT 1391

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides methods for control, management, treatment and prevention of conditions related to **nitric oxide** deficiency such as hypertension, cardiovascular disease, osteoporosis, diabetes mellitus, preeclampsia HELLP, syndrome and fetal growth retardation; uterine contractility disorders such as preterm labor and dysmenorrhea, cervical dystocia, infertility and early pregnancy loss; male impotence; urinary incontinence; intestinal tract disorders (e.g. altered motility and pyloric stenosis), respiratory system diseases (e.g. asthma, neonatal respiratory distress syndrome, pulmonary hypertension, and adult respiratory distress syndrome); inflammatory diseases (e.g. acute inflammation, resistance to infection, SLE-lupus, anaphylactic reaction, allograft rejection); Alzheimer's disease, stroke, growth hormone disorders, and behavior changes; dermatological conditions such as atopic eczema, topical hair loss, and burn injury; by administering citrulline or a citrulline analogue, optionally in combination with other enhancing or modulating agents, e.g., an estrogenic, partial estrogenic, progestagenic, or androgenic agent, and pharmaceutical preparations for such uses.

L10 ANSWER 4 OF 38 USPATFULL

AN 2001:217985 USPATFULL

TI Infrared thermography and methods of use

IN Marek, Przemyslaw A., Bolton, MA, United States

Trocha, Andzrej M., Billerica, MA, United States

PI US 2001046471 A1 20011129

AI US 2001-850081 A1 20010508 (9)

PRAI US 2000-202935P 20000509 (60)

DT Utility

FS APPLICATION

LREP EDWARD D GRIEFF, HALE & DORR LLP, 1455 PENNSYLVANIA AVE, NW, WASHINGTON,

DC, 20004

CLMN Number of Claims: 99

ECL Exemplary Claim: 1

DRWN 6 Drawing Page(s)

LN.CNT 2687

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention describes rapid noninvasive methods for measuring vasodilation or changes in blood flow in a patient following administration of at least one compound that donates, transfers or

releases **nitric oxide**, elevates endogenous levels of **endothelium**-derived relaxing factor, stimulates endogenous synthesis of **nitric oxide** or is a substrate for **nitric oxide** synthase and/or at least one vasoactive agent. The method comprises the administration of at least one compound that donates, transfers or releases **nitric oxide**, elevates endogenous levels of **endothelium**-derived relaxing factor, stimulates endogenous synthesis of **nitric oxide** or is a substrate for **nitric oxide** synthase and/or at least one vasoactive agent to the patient followed by monitoring the temperature change of an area of interest using infrared thermography. The present invention provides methods for diagnosing diseases or disorders related to vasodilation and changes in blood flow, such as, sexual dysfunction, Raynaud's syndrome, inflammation, hypertension, gastrointestinal disorders and central nervous system disorders. The sexual dysfunction is preferably female sexual dysfunction and female sexual arousal. The vasoactive agents include potassium channel activators, calcium channel blockers, .alpha.-adrenergic receptor antagonists, .beta.-blockers, phosphodiesterase inhibitors, adenosine, ergot alkaloids, vasoactive intestinal peptides, prostaglandins, dopamine agonists, opioid antagonists, endothelin antagonists and thromboxane inhibitors. The present invention can also be used to screen and identify drug candidates for treating diseases, disorders and conditions resulting from vasodilation or changes in blood flow. The present invention also describes compositions comprising at least one S-nitrosothiol compound for diagnosing, monitoring and/or treating female sexual dysfunctions.

L10 ANSWER 5 OF 38 USPATFULL

AN 2001:182568 USPATFULL

TI Therapies using hemoproteins

IN Stamler, Jonathan S., Chapel Hill, NC, United States

Hausladen, Alfred, Durham, NC, United States

PA Duke University Medical Center, Durham, NC, United States, 27708-0083 (non-U.S. corporation)

PI US 2001031727 A1 20011018

AI US 2001-756478 A1 20010108 (9)

RLI Continuation of Ser. No. WO 1999-US15487, filed on 9 Jul 1999, UNKNOWN

PRAI US 1998-92372P 19980710 (60)

DT Utility

FS APPLICATION

LREP David E. Brook, Esq., HAMILTON, BROOK, SMITH & REYNOLDS, P.C., Two Militia Drive, Lexington, MA, 02421-4799

CLMN Number of Claims: 57

ECL Exemplary Claim: 1

DRWN 35 Drawing Page(s)

LN.CNT 2144

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Herein it is shown that hemoproteins (e.g., Ascaris hemoglobin, myoglobin, flavohemoglobins) have NO-consuming and deoxygenase activities. The invention provides a method of reducing the concentration of oxygen and/or **nitric oxide** in a mammal. The method of the invention comprises administering a therapeutically effective amount of a hemoprotein having NO-activated deoxygenase activity or an enzymatically active fragment thereof to a mammal. The method can be used to treat a mammal having pathologically proliferating cells, such as a tumor. In one embodiment, the hemoprotein is administered to reduce the oxygen concentration of a tumor. In another embodiment, the hemoprotein is administered together with a cytotoxic agent to treat a mammal having a tumor. The invention also provides a method of enzymatically generating toxic reactive oxygen species in a mammal for therapeutic purposes. The method comprises administering a therapeutically effective amount of a hemoprotein to a mammal. The invention also provides a composition comprising a

hemoprotein having deoxygenase activity or an enzymatically active fragment thereof and a physiologically acceptable carrier. In one embodiment, the composition further comprises a cytotoxic agent and/or a reducing agent. The invention further provides a method of treating a mammal infected with *Ascaris* sp., comprising administering to said mammal a therapeutically effective amount of an inhibitor of NO synthase. The NO-consuming activity of a hemoprotein (e.g., a flavohemoglobin) can be used in a treatment where constriction of blood vessels is desirable, or where it is otherwise desirable to reduce NO concentration, as in inflammation.

L10 ANSWER 6 OF 38 USPATFULL  
AN 2001:152517 USPATFULL  
TI Topical **nitric oxide** donor compositions  
IN Russell, Meri Charmyne, 206 SW. 42nd St., Des Moines, IA, United States 50312  
PA Russell, Meri Charmyne, Johnston, IA, United States (U.S. individual)  
PI US 6287601 B1 20010911  
AI US 1999-333974 19990616 (9)  
RLI Continuation of Ser. No. US 1997-914230, filed on 19 Aug 1997, now patented, Pat. No. US 6045827 Division of Ser. No. US 1996-752415, filed on 19 Nov 1996, now patented, Pat. No. US 5891472  
DT Utility  
FS GRANTED  
EXNAM Primary Examiner: Levy, Neil S.  
LREP Peppper Hamilton LLP, Villarcorta, Gilberto M., Pauliquen, Corinne M.  
CLMN Number of Claims: 19  
ECL Exemplary Claim: 1  
DRWN 3 Drawing Figure(s); 2 Drawing Page(s)  
LN.CNT 817  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB Compositions and methods of the topical treatment of equine laminitis are disclosed. In particular, combinations of a fast acting **nitric oxide** (NO) donor, a sustained acting NO donor and an NSAID mixed in a lipid-based carrier are described. The application of such combinations to the affected areas, e.g., the hoofs and surrounding tissues, of an equine afflicted with laminitis provides relief from the debilitating effects of this painful, often life-threatening condition.

L10 ANSWER 7 OF 38 USPATFULL  
AN 2001:117026 USPATFULL  
TI Use of **nitric oxide** scavengers to treat side effects caused by therapeutic administration of sources of **nitric oxide**  
IN Lai, Ching-San, Encinitas, CA, United States  
PA Medinox, Inc., San Diego, CA, United States (U.S. corporation)  
PI US 6265420 B1 20010724  
AI US 1998-103640 19980623 (9)  
DT Utility  
FS GRANTED  
EXNAM Primary Examiner: Kight, John; Assistant Examiner: Faulkner, D.  
LREP Gray Cary Ware & Freidenrich LLP, Reiter, Stephen E., Learn, June M.  
CLMN Number of Claims: 56  
ECL Exemplary Claim: 1  
DRWN 2 Drawing Figure(s); 1 Drawing Page(s)  
LN.CNT 1157  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB **Nitric oxide** scavengers, such as dithiocarbamate-containing compounds, are used to reduce side effects caused by therapeutic administration of **nitric oxide** sources by administering the **nitric oxide** scavenger(s) to the subject after the therapeutic effect of the **nitric oxide** source has been achieved. For example,

the **nitric oxide** source can be coadministered with the **nitric oxide** scavenger, with the latter formulated in a time release vehicle selected to delay release of the scavenger for a period of time sufficient to ensure that the therapeutic goal of the **nitric oxide** source has been achieved before release of the scavenger. Formulations and kits, including a bubble pack with pairwise arrangement of unit doses of a desired **nitric oxide** source and **nitric oxide** scavenger, are also provided. The side effects of sildenafil citrate (Viagra.RTM.), or of simultaneous administration of such a **nitric oxide** source in combination with another, such as nitroglycerin, are effectively controlled by the methods, formulations and kits of the invention.

L10 ANSWER 8 OF 38 USPATFULL

AN 2001:102806 USPATFULL

TI Composition and method for treating a patient susceptible to or suffering from a cardiovascular disorder or disease

IN Daniels, Bruce A., Oklahoma City, OK, United States

PA EndoMatrix, Inc., Napa, CA, United States (U.S. corporation)

PI US 6255296 B1 20010703

AI US 1999-302690 19990430 (9)

RLI Continuation-in-part of Ser. No. US 1996-585743, filed on 16 Jan 1996, now abandoned Continuation of Ser. No. US 1994-180131, filed on 11 Jan 1994, now abandoned

DT Utility

FS GRANTED

EXNAM Primary Examiner: Padmanabhan, Sreeni

LREP Lanahan & Reilley LLP, Gregory, Draper B.

CLMN Number of Claims: 17

ECL Exemplary Claim: 1

DRWN 11 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 861

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for inhibiting the effects of cardiovascular disorders and diseases in a host susceptible to or suffering from a cardiovascular disorder or disease comprising administering to the host, a therapeutically effective amount of a first substance characterized as simulating a heparin-like effect, and a therapeutically effective amount of a second substance characterized as simulating an arginine-like effect; and a formulation for use in treating a host susceptible to or suffering from the effects of cardiovascular disorders and diseases comprising a therapeutically effective amount of a first substance characterized as simulating a heparin-like effect, and a second substance characterized as simulating an arginine-like effect, as described.

L10 ANSWER 9 OF 38 USPATFULL

AN 2001:43748 USPATFULL

TI Dosage forms for the treatment of the chronic glaucomas

IN Richardson, Kenneth T., Anchorage, AK, United States

Pearson, Don C., Lakewood, WA, United States

PA ChronoRX, LLC, Anchorage, AK, United States (U.S. corporation)

PI US 6207190 B1 20010327

AI US 1999-372362 19990811 (9)

PRAI US 1998-96658P 19980813 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Spear, James M.

LREP Townsend and Townsend and Crew LLP

CLMN Number of Claims: 56

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1808

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Four interdependent functional groups of biofactors and biomolecules are identified and formulations are defined which are comprised of their members. The active agents are demonstrated to be complementary in their physiological functions especially as these relate to endothelial biochemistry and physiology, hyperinsulinemia and, ultimately, to vascular health. The active components of the invention are selected for inclusion in precise combinations that reduce a variety of risks of vasculopathy in addition to reducing intraocular pressure. Widespread systemic improvement associated with local, optic nerve betterment of vascular health, reduces the risk of optic nerve atrophy with its accompanying visual field loss and potential blindness. The reduction of this maximizes the potential clinical therapeutic success of current medical, IOP-lowering, anti-glaucoma mediations.

L10 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2002 ACS

AN 2000:666601 CAPLUS

DN 133:256811

TI Pharmaceutical compositions containing dopamine agonists in combination with **nitric oxide** donors for treating and/or preventing sexual dysfunctions

IN Garvey, David S.

PA Nitromed, Inc., USA

SO PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000054773	A1	20000921	WO 2000-US3709	20000310
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRAI US 1999-123920P P 19990312

OS MARPAT 133:256811

AB The present invention is directed to novel compns. comprising at least one dopamine agonist in combination with at least one **nitric oxide** donor (i.e. compds. that donate, transfer or release **nitric oxide**, elevate endogenous levels of **endothelium**-derived relaxing factor, stimulate endogenous synthesis of **nitric oxide** or are substrates for **nitric oxide** synthase). The novel compns. may optionally comprise at least one therapeutic agent, such as, a vasoactive agent, an antiemetic agent, and mixts. thereof. The dopamine agonist is preferably apomorphine. The present invention is also directed to methods for treating and/or preventing sexual dysfunctions and/or enhancing sexual responses in patients. In other embodiments, the present invention is directed to methods treating or preventing neurodegenerative diseases, mitochondrial diseases, spinal cord injury, central or psychostimulant addiction, senile dementia, circulatory disorders, cardiovascular disorders, hyperprolactinemia or myopia. The compds. and/or compns. of the present invention can also be provided in the form of a pharmaceutical kit (no data).

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 38 USPATFULL

AN 2000:138405 USPATFULL  
TI Treatment of osteoporosis and metabolic bone disorders with  
**nitric oxide** substrate and/or donors  
IN Yallampalli, Chandrasekhar, Houston, TX, United States  
Wimalawansa, Sunil J., Friendswood, TX, United States  
PA Board of Regents, The University of Texas System, United States (U.S.  
corporation)  
PI US 6133320 20001017  
AI US 1998-177978 19981022 (9)  
RLI Division of Ser. No. US 1996-616470, filed on 19 Mar 1996, now patented,  
Pat. No. US 5898038  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Criares, Theodore J.  
LREP Fulbright & Jaworski  
CLMN Number of Claims: 98  
ECL Exemplary Claim: 1  
DRWN 3 Drawing Figure(s); 2 Drawing Page(s)  
LN.CNT 794

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Primary and secondary osteoporosis in a female or a male mammal is  
treated by administering thereto a **nitric oxide**  
synthase substrate, a **nitric oxide** donor or both,  
optionally; in further combination with one or more of an estrogen, a  
progestin, an anabolic steroid. **Nitric oxide**  
substrate or donor also can be combined with one or more of other  
medications acting on bone, such as bisphosphonate, calcitonin,  
fluoride, androgen and other novel therapeutic agents. Either  
**nitric oxide** donor or substrate by itself or  
combination with other medications as described above can be used in  
both women and men, (preferably human) for prevention and treatment of  
osteoporosis and other metabolic bone disorders.

L10 ANSWER 12 OF 38 USPATFULL

AN 2000:40672 USPATFULL  
TI Treatment of equine laminitis  
IN Russell, Meri Charmyne, 206 SW. 42nd St., Des Moines, IA, United States  
50312  
PA Russell, Meri Charmyne, Des Moines, IA, United States (U.S. individual)  
PI US 6045827 20000404  
AI US 1997-914230 19970819 (8)  
RLI Division of Ser. No. US 1996-752415, filed on 19 Nov 1996  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Levy, Neil S.  
LREP Villacorta, Gilberto M. Pepper Hamilton LLP  
CLMN Number of Claims: 19  
ECL Exemplary Claim: 1  
DRWN 3 Drawing Figure(s); 2 Drawing Page(s)  
LN.CNT 828

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compositions and methods of the topical treatment of equine laminitis  
are disclosed. In particular, combinations of a fast acting  
**nitric oxide** (NO) donor, a sustained acting NO donor  
and an NSAID mixed in a lipid-based carrier are described. The  
application of such combinations to the affected areas, e.g., the hoofs  
and surrounding tissues, of an equine afflicted with laminitis provides  
relief from the debilitating effects of this painful, often  
life-threatening condition.

L10 ANSWER 13 OF 38 USPATFULL

AN 2000:34586 USPATFULL  
TI Implantation rates after in vitro fertilization, treatment of  
infertility and early pregnancy loss with a **nitric**

**oxide** donor alone or in combination with progesterone, and a method for contraception with **nitric oxide** inhibitors

IN Chwalisz, Krzysztof, Berlin, Germany, Federal Republic of  
Garfield, Robert E., Friendswood, TX, United States  
PA Schering Aktiengesellschaft, Berlin, Germany, Federal Republic of  
(non-U.S. corporation)  
The Board of Regents, Univ. of Texas System, Austin, TX, United States  
(U.S. corporation)  
PI US 6040340 20000321  
AI US 1996-646518 19960507 (8)  
DT Utility  
FS Granted  
EXNAM Primary Examiner: MacMillan, Keith D.  
LREP Millen, White, Zelano & Branigan, P.C.  
CLMN Number of Claims: 27  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)  
LN.CNT 756

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is provided for the improvement of implantation rates and/or pregnancy rates in a female mammal, comprising administering to a female mammal in whom pregnancy is desired an effective amount of

(a) a **nitric oxide** synthase substrate, a **nitric oxide** donor, or both, optionally in combination with

(b) a progestin, and,

(c) optionally, in further combination with an estrogen.

A method is also provided for fertility control for a female mammal, comprising administering to a female mammal in whom pregnancy is not desired and at risk for becoming pregnant an effective amount of **nitric oxide** synthase inhibitor in combination with an antiprogestin. Pharmaceutical compositions are also provided.

L10 ANSWER 14 OF 38 USPATFULL

AN 1999:124865 USPATFULL  
TI Treatment of preeclampsia and preterm labor with combination of  
progestational agent and a **nitric oxide** synthase  
substrate and/or donor  
IN Garfield, Robert E., Friendswood, TX, United States  
Chwalisz, Krzysztof, Berlin, Germany, Federal Republic of  
Bukowski, Radoslaw, Berlin, Germany, Federal Republic of  
Yallamp'al Li, Chandra, Houston, TX, United States  
PA The Board of Regents, University of Texas, Galveston, TX, United States  
(U.S. corporation)  
Schering Aktiengesellschaft, Germany, Federal Republic of (non-U.S.  
corporation)  
PI US 5965529 19991012  
AI US 1995-466688 19950606 (8)  
RLI Continuation of Ser. No. US 1993-92426, filed on 16 Jul 1993  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Lilling, Herbert J.  
LREP Millen, White, Zelano, & Branigan, P.C.  
CLMN Number of Claims: 32  
ECL Exemplary Claim: 1  
DRWN 10 Drawing Figure(s); 6 Drawing Page(s)  
LN.CNT 600

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Preeclampsia and preterm labor in a pregnant female mammal are treated

by administering thereto a combination of a progestin and a **nitric oxide** synthase substrate, a **nitric oxide** donor or both, optionally in further combination with one or more of a cyclooxygenase inhibitor, a PGI.sub.2 -mimetic, a thromboxane (TXA.sub.2) inhibitor, a compound possessing TXA.sub.2 -agonistic and TXA.sub.2 -inhibiting properties, a compound possessing TXA.sub.2 -antagonistic and PGI.sub.2 -mimetic activities, and a TXA.sub.2 antagonist.

L10 ANSWER 15 OF 38 USPATFULL

AN 1999:117449 USPATFULL

TI Treatment of climacteric disorders with **nitric oxide** synthase substrates and/or donors

IN Garfield, Robert E., Friendswood, TX, United States  
Chwalisz, Krzysztof, Berlin, Germany, Federal Republic of  
Bukowski, Radoslaw, Berlin, Germany, Federal Republic of  
Yallampalli, Chandra, Houston, TX, United States

PA Schering Aktiengesellschaft, Germany, Federal Republic of (non-U.S. corporation)  
Board of Regents, University of Texas, Austin, TX, United States (U.S. corporation)

PI US 5958878 19990928

AI US 1995-466538 19950606 (8)

RLI Continuation of Ser. No. US 1993-153345, filed on 16 Nov 1993, now patented, Pat. No. US 5595970 which is a continuation-in-part of Ser. No. US 1993-92426, filed on 16 Jul 1993

DT Utility

FS Granted

EXNAM Primary Examiner: Lankford, Jr., Leon B.; Assistant Examiner: Tate, Christopher R.

LREP Miller, White, Zelano & Branigan, P.C.

CLMN Number of Claims: 34

ECL Exemplary Claim: 1

DRWN 4 Drawing Figure(s); 2 Drawing Page(s)

LN.CNT 644

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The symptoms of the climacterium are ameliorated by the administration to an afflicted individual one or both of a **nitric oxide** substrate and/or nitric acid donor, alone or optionally in combination with a progestin or, in the case of a non-pregnant female, either a progestin or an estrogen or both.

L10 ANSWER 16 OF 38 USPATFULL

AN 1999:65238 USPATFULL

TI Treatment or prevention of preeclampsia, eclampsia with calcitonin gene related peptide, CGRP analog, prostaglandin agent, **nitric oxide** source, and cyclooxygenase inhibitor

IN Yallampalli, Chandrasekhar, Houston, TX, United States  
Wimalawansa, Sunil J., Friendswood, TX, United States

PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)

PI US 5910482 19990608

AI US 1996-619841 19960319 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Delaney, Patrick R.

LREP Arnold White & Durkee

CLMN Number of Claims: 32

ECL Exemplary Claim: 1

DRWN 5 Drawing Figure(s); 5 Drawing Page(s)

LN.CNT 770

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a method for counteracting preeclampsia,

eclampsia of pregnancy and preterm labor in a pregnant female mammal treated by administering thereto calcitonin gene-related peptide (CGRP) or its analogues including CGRP/adrenomedullin or their peptide or receptor-based analogues, or in combination with a progestin, and with or without a **nitric oxide** substrate, or a **nitric oxide** donor or both, optionally in further combination with one or more of a cyclooxygenase inhibitor, a PGI.sub.2 -mimetic, a thromboxane (TXA.sub.2) inhibitor, a compound possessing TXA.sub.2 -agonistic, and TXA.sub.2 -inhibiting properties, a compound possessing TXA.sub.2 -antagonistic and PGI.sub.2 -mimetic activities, and a TXA.sub.2 antagonist. CGRP, progesterone and some of the **nitric oxide** substrate and donor compounds are naturally occurring compounds. As such these agents do not have the same toxicity and allergy problems as the foreign substances that are currently used for similar purposes. During pregnancy uterine blood vessels and the uterine muscles are particularly sensitive to CGRP as well as **nitric oxide**. Therefore, one could administer a very small quantities of these drugs (i.e., intravenously, subcutaneous, or Implants), the effects are then seen mainly in the uterine muscle and blood vessels, namely increase the blood supply to the uteroplacental unit (hence nutrients and oxygen supply to the fetus through the improved placental circulation), and uterine muscular relaxation thereby ameliorate the signs and symptoms of preeclampsia, and eclampsia, and prevent preterm labor. At these dosages, virtually no systemic effects are induced, making CGRP (which is an endogenous natural product present in human body) extremely safe and effective.

L10 ANSWER 17 OF 38 USPATFULL

AN 1999:61173 USPATFULL

TI Treatment of male climacteric disorders with **nitric oxide** synthase substrates and/or donors, in combination with androgens and/or aromatase inhibitors

IN Chwalisz, Kristof, Berlin, Germany, Federal Republic of Garfield, Robert E., Friendswood, TX, United States

PA Schering Aktiengesellschaft and Board of Regents, Berlin, Germany, Federal Republic of (non-U.S. corporation)  
The University of Texas System, Austin, TX, United States (U.S. corporation)

PI US 5906987 19990525

AI US 1997-812912 19970310 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Jordan, Kimberly

LREP Millen, White, Zelano & Branigan, P.C.

CLMN Number of Claims: 30

ECL Exemplary Claim: 1

DRWN 2 Drawing Figure(s); 2 Drawing Page(s)

LN.CNT 689

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The symptoms of climacterium in male mammals, e.g., hypertension, cardiovascular disease and osteoporosis, are ameliorated by the administration to an afflicted individual one or both of a **nitric oxide** substrate and/or nitric acid donor, in combination with an androgen, an aromatase inhibitor or both, wherein the circulating levels of testosterone in the afflicted individual are increased.

L10 ANSWER 18 OF 38 USPATFULL

AN 1999:50846 USPATFULL

TI Treatment of osteoporosis and metabolic bone disorders with **nitric oxide** substrate and/or donors

IN Yallampalli, Chandrasekhar, Houston, TX, United States  
Wimalawansa, Sunil J., Friendswood, TX, United States

PA Board of Regents, The University of Texas System, Austin, TX, United

States (U.S. corporation)  
PI US 5898038 19990427  
AI US 1996-616470 19960319 (8)  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Criares, Theodore J.  
LREP Arnold, White & Durkee  
CLMN Number of Claims: 50  
ECL Exemplary Claim: 1  
DRWN 3 Drawing Figure(s); 2 Drawing Page(s)  
LN.CNT 669

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Primary and secondary osteoporosis in a female or a male mammal is treated by administering thereto a **nitric oxide** synthase substrate, a **nitric oxide** donor or both, optionally; in further combination with one or more of an estrogen, a progestin, an anabolic steroid. **Nitric oxide** substrate or donor also can be combined with one or more of other medications acting on bone, such as bisphosphonate, calcitonin, fluoride, androgen and other novel therapeutic agents. Either **nitric oxide** donor or substrate by itself or combination with other medications as described above can be used in both women and men, (preferably human) for prevention and treatment of osteoporosis and other metabolic bone disorders.

L10 ANSWER 19 OF 38 USPATFULL

AN 1999:48230 USPATFULL

TI Treatment of preeclampsia and preterm labor with combination of gestational agent and a **nitric oxide** synthase substrate and/or donor

IN Garfield, Robert E., Friendswood, TX, United States  
Chwalisz, Krzysztof, Berlin, Germany, Federal Republic of  
Bukowski, Radoslaw, Berlin, Germany, Federal Republic of  
Yallampal Li, Chandra, Houston, TX, United States

PA Schering Aktiengesellschaft, Germany, Federal Republic of (non-U.S. corporation)  
The University of Texas, Austin, TX, United States (U.S. corporation)

PI US 5895783 19990420  
AI US 1993-92426 19930716 (8)  
DT Utility  
FS Granted

EXNAM Primary Examiner: Lilling, Herbert J.  
LREP Millen, White, Zelano & Branigan, P.C.  
CLMN Number of Claims: 22  
ECL Exemplary Claim: 1  
DRWN 10 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 556

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Preeclampsia and preterm labor in a pregnant female mammal are treated by administering thereto a combination of a progestin and a **nitric oxide** synthase substrate, a **nitric oxide** donor or both, optionally in further combination with one or more of a cyclooxygenase inhibitor, a PGI.sub.2 -mimetic, a thromboxane (TXA.sub.2) inhibitor, a compound possessing TXA.sub.2 -agonistic and TXA.sub.2 -inhibiting properties, a compound possessing TXA.sub.2 -antagonistic and PGI.sub.2 -mimetic activities, and a TXA.sub.2 antagonist.

L10 ANSWER 20 OF 38 USPATFULL

AN 1999:43221 USPATFULL

TI Treatment of equine laminitis

IN Russell, Meri Charmyne, 206 SW. 42nd St., Des Moines, IA, United States  
50312

PA Russell, Meri Charmyne, Des Moines, IA, United States (U.S. individual)

PI US 5891472 19990406  
AI US 1996-752415 19961119 (8)  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Levy, Neil S.  
LREP Villacorta, Gilberto M. Pepper Hamilton LLP  
CLMN Number of Claims: 13  
ECL Exemplary Claim: 1  
DRWN 3 Drawing Figure(s); 2 Drawing Page(s)  
LN.CNT 810

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compositions and methods of the topical treatment of equine laminitis are disclosed. In particular, combinations of a fast acting **nitric oxide** (NO) donor, a sustained acting NO donor and an NSAID mixed in a lipid-based carrier are described. The application of such combinations to the affected areas, e.g., the hoofs and surrounding tissues, of an equine afflicted with laminitis provides relief from the debilitating effects of this painful, often life-threatening condition.

L10 ANSWER 21 OF 38 USPATFULL

AN 1999:7156 USPATFULL

TI Intramural delivery of **nitric oxide** enhancer for inhibiting lesion formation after vascular injury

IN Cooke, John P., Palo Alto, CA, United States  
Schwarzacher, Sverin, Menlo Park, CA, United States  
Lim, Tai T., Singapore, Singapore  
Yeung, Alan C., Hillsborough, CA, United States

PA The Board of Trustees of the Leland Stanford Junior University, Stanford, CA, United States (U.S. corporation)

PI US 5861168 19990119

AI US 1996-764919 19961216 (8)

RLI Continuation-in-part of Ser. No. US 1996-695792, filed on 12 Aug 1996 which is a continuation-in-part of Ser. No. US 1995-556035, filed on 9 Nov 1995 which is a continuation-in-part of Ser. No. US 1994-336159, filed on 8 Nov 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-76312, filed on 11 Jun 1993, now patented, Pat. No. US 5428070

DT Utility

FS Granted

EXNAM Primary Examiner: Russel, Jeffrey E.

CLMN Number of Claims: 8

ECL Exemplary Claim: 1

DRWN 15 Drawing Figure(s); 12 Drawing Page(s)

LN.CNT 734

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Vessels suffering vascular injury from angioplasty are treated with L-arginine intramurally. The incidents associated with restenosis are substantially reduced providing for a reduced incidence of restenosis as a result of the injury.

L10 ANSWER 22 OF 38 USPATFULL

AN 1999:1496 USPATFULL

TI Purified **nitric oxide** synthase from rat brain

IN Rosazza, John P. N., Iowa City, IA, United States  
Chen, Yijun, Iowa City, IA, United States

PA University of Iowa Research Foundation, Iowa City, IA, United States (U.S. corporation)

PI US 5856158 19990105

AI US 1996-675821 19960705 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Weber, Jon P.; Assistant Examiner: Hanley, Susan

LREP Zarley, McKee, Thomte, Voorhees & Sease

CLMN Number of Claims: 7  
ECL Exemplary Claim: 1  
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)  
LN.CNT 1497

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A **nitric oxide** synthase (NOS) protein is obtained from rat brain and purified to a specific activity at least 6,360-fold that of a crude tissue preparation. The NOS protein has a denatured MW of 105 kD determined by SDS-PAGE, a dimeric MW of 230 kD determined by gel filtration and requires FAD, FMN, Ca.sup.2+ and tetrahydropterin for the production of **nitric oxide** from L-arginine or an arginine-rich peptide, oligopeptide or protein substrate.

L10 ANSWER 23 OF 38 USPATFULL

AN 1998:154309 USPATFULL

TI Method for in vivo reduction of **nitric oxide** levels and compositions useful therefor

IN Lai, Ching-San, Encinitas, CA, United States

PA MCW Research Foundation, Milwaukee, WI, United States (U.S. corporation)

PI US 5847004 19981208

AI US 1996-767125 19961209 (8)

RLI Continuation-in-part of Ser. No. US 1995-554196, filed on 6 Nov 1995 which is a continuation-in-part of Ser. No. US 1995-459518, filed on 2 Jun 1995, now patented, Pat. No. US 5741815

DT Utility

FS Granted

EXNAM Primary Examiner: Rotman, Alan L.; Assistant Examiner: Smith, Lyman H.

LREP Gray Cary Ware and Freidenrich, Reiter, Stephen E.

CLMN Number of Claims: 33

ECL Exemplary Claim: 1

DRWN 13 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 1485

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In accordance with the present invention, there are provided methods for the in vivo reduction of **nitric oxide** levels in a mammalian subject. In contrast to the inhibitory approach described in the prior art (i.e., wherein the function of the enzymes responsible for **nitric oxide** production is inhibited), the present invention employs a scavenging approach whereby overproduced **nitric oxide** is bound in vivo to a suitable **nitric oxide** scavenger. The resulting complex renders the **nitric oxide** harmless, and is eventually excreted in the urine of the host. An exemplary **nitric oxide** scavenger contemplated for use in the practice of the present invention is a dithiocarbamate-ferrous iron complex. This complex binds to .NO, forming a stable, water-soluble NO-containing complex having a characteristic three-line spectrum (indicative of a mononitrosyl-Fe complex) which can readily be detected at ambient temperatures by electron paramagnetic resonance (EPR) spectroscopy. The present invention relates to methods for reducing in vivo levels of .NO as a means of treating subjects afflicted with inflammatory and/or infectious disease. **Nitric oxide** scavengers are administered to a host in need of such treatment; these scavengers interact with in vivo produced .NO, forming a stable NO-containing complex. The NO-containing complex is then filtered through the kidneys, concentrated in the urine, and eventually excreted by the subject, thereby reducing in vivo .NO levels.

L10 ANSWER 24 OF 38 USPATFULL

AN 1998:22208 USPATFULL

TI Preventing conversion of citrulline to argininosuccinate to limit pathological **nitric oxide** overproduction

IN Gross, Steven S., New York, NY, United States

Griffith, Owen W., Milwaukee, WI, United States

PA The Medical College of Wisconsin Research Foundation, Milwaukee, WI,  
United States (U.S. corporation)  
PI US 5723448 19980303  
AI US 1996-618810 19960320 (8)  
RLI Division of Ser. No. US 1994-354585, filed on 12 Dec 1994, now patented,  
Pat. No. US 5545625  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Jordan, Kimberly  
CLMN Number of Claims: 13  
ECL Exemplary Claim: 1  
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)  
LN.CNT 1069

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Administration of argininosuccinate synthetase activity reducing agents,  
e.g., argininosuccinate synthetase induction blocking agents (e.g.,  
antibiotics that bind to DNA sequences present in the upstream  
regulatory region of the argininosuccinate synthetase gene, such as  
mithramycin) and argininosuccinate synthetase inhibitors (e.g.,  
L-citrulline antagonists such as methyl citrulline and L-aspartate  
antagonists such as D-aspartate) is useful to prevent or treat sepsis or  
cytokine-induced systemic hypotension, is useful in the treatment of  
sepsis or cytokine-induced systemic hypotension to restore vascular  
sensitivity to the effects of  $\alpha$ -adrenergic agonists, and is  
useful to suppress an immune response, e.g., in treating inflammation.  
In one embodiment, certain argininosuccinate synthetase activity  
reducing agents are used together with arginine antagonists to treat  
sepsis or cytokine induced hypotension.

L10 ANSWER 25 OF 38 USPATFULL

AN 1998:19743 USPATFULL

TI Ovulation control by regulating **nitric oxide** levels

IN Garfield, Robert E., Friendswood, TX, United States

Yallampalli, Chandrasekhar, Houston, TX, United States

PA Board of Regents, The University of Texas System, Austin, TX, United  
States (U.S. corporation)

PI US 5721278 19980224

AI US 1995-477187 19950607 (8)

RLI Division of Ser. No. US 1993-165309, filed on 10 Dec 1993, now patented,  
Pat. No. US 5470847

DT Utility

FS Granted

EXNAM Primary Examiner: Criares, Theodore J.

LREP Arnold, White & Durkee

CLMN Number of Claims: 4

ECL Exemplary Claim: 1

DRWN 1 Drawing Figure(s); 1 Drawing Page(s)

LN.CNT 556

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Inhibition of ovulation in a female may be achieved by administering a  
**nitric oxide** synthase inhibitor, alone or in  
combination with one or more of a progestin, an estrogen, and an LH-RH  
antagonist, thereby preventing conception. The stimulation of ovulation  
in a female may be achieved by administering a **nitric**  
**oxide** source, optionally in further combination with one or more  
of clomiphene, a gonadotropin, and an LH-RH agonist.

L10 ANSWER 26 OF 38 USPATFULL

AN 97:56710 USPATFULL

TI Ovulation control by regulating **nitric oxide** levels

IN Garfield, Robert E., Friendswood, TX, United States

Yallampalli, Chandrasekhar, Houston, TX, United States

PA Board of Regents, The University of Texas System, Austin, TX, United  
States (U.S. corporation)

PI US 5643944 19970701  
AI US 1995-477189 19950607 (8)  
RLI Division of Ser. No. US 1993-165309, filed on 10 Dec 1993, now patented,  
Pat. No. US 5470847  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Criares, Theodore J.  
LREP Arnold White & Durkee  
CLMN Number of Claims: 3  
ECL Exemplary Claim: 1  
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)  
LN.CNT 571

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The stimulation of ovulation in a female may be achieved by  
administering a **nitric oxide** source, optionally in  
further combination with one or more of clomiphene, a gonadotropin, and  
an LH-RH agonist.

L10 ANSWER 27 OF 38 USPATFULL

AN 97:5950 USPATFULL

TI Treatment of climacteric disorders with **nitric oxide**  
synthase substrates and/or donors

IN Garfield, Robert E., Friendswood, TX, United States  
Chwalisz, Krzysztof, Berlin, Germany, Federal Republic of  
Bukowski, Radoslaw, Berlin, Germany, Federal Republic of  
Yallampalli, Chandra, Houston, TX, United States

PA Schering Aktiengesellschaft, Berlin, Germany, Federal Republic of  
(non-U.S. corporation)

PI US 5595970 19970121

AI US 1993-153345 19931116 (8)

RLI Continuation-in-part of Ser. No. US 1993-92426, filed on 16 Jul 1993,  
now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Lilling, Herbert J.

LREP Millen, White, Zelano & Branigan, P.C.

CLMN Number of Claims: 14

ECL Exemplary Claim: 1

DRWN 4 Drawing Figure(s); 2 Drawing Page(s)

LN.CNT 562

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The symptoms of the climacterium are ameliorated by the administration  
to an afflicted individual one or both of a **nitric**  
**oxide** substrate and/or nitric acid donor, alone or optionally in  
combination with a progestin or, in the case of a non-pregnant female,  
either a progestin or an estrogen or both.

L10 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1

AN 1997:242796 CAPLUS

DN 126:258857

TI Effects of L-arginine and N.omega.-nitro-L-arginine methyl ester on  
cardiac perfusion and function after 1-day cold preservation of isolated  
hearts

AU Stowe, David F.; Boban, Mladen; Roerig, David L.; Chang, David; Palmisano,  
Barbara W.; Bosnjak, Zeljko J.

CS Anesthesiology Research Laboratory, Departments of Anesthesiology,  
Cardiovascular Research Center, Medical College of Wisconsin, Milwaukee,  
WI, 53226, USA

SO Circulation (1997), 95(6), 1623-1634

CODEN: CIRCAZ; ISSN: 0009-7322

PB American Heart Association

DT Journal

LA English

AB Coronary flow responses to **endothelium**-dependent (acetylcholine

[ACh] or 5-hydroxytryptamine [5-HT]) and **endothelium**-independent (adenosine [ADE] or nitroprusside [NP]) vasodilators may be altered before and after 1-day hypothermia during the perfusion of arginine vasopressin (AVP), D-arginine (D-ARG), L-arginine (L-ARG), or nitro-L-arginine Me ester (L-NAME). Four groups of guinea pig hearts (37.5.degree.C [warm]) were perfused for 6 h with AVP, L-ARG, L-NAME, or nothing (control). Five heart groups (cold) were perfused with AVP, D-ARG, L-ARG, L-NAME, or nothing (control), but after 2 h they were perfused at low flow for 22 h at 3.7.degree.C and again for 3 h at 37.5.degree.C. ADE, butanedione monoxime, and NP were given for cardioprotection before, during, and after hypothermia. In warm groups, L-ARG did not alter basal flow or ADE, ACh, 5-HT, or NP responses, whereas L-NAME and AVP reduced basal flow and the ADE response, abolished ACh and 5-HT responses, and increased the NP response. In cold groups after hypothermia, L-ARG did not alter basal flow, but L-NAME, AVP, D-ARG, and control reduced flow. In the postcold L-ARG group, ACh increased peak flow, but NP did not increase flow in other cold groups. Effluent L-ARG and L-CIT in the cold control group fell from 64. $\pm$ .9 and 9. $\pm$ .1  $\mu$ g/L at 1 h to 36. $\pm$ .5 and 5. $\pm$ .1  $\mu$ g/L at 25 h, resp. Left ventricular pressure and cardiac efficiency improved more in the postcold L-ARG group than in the postcold D-ARG, AVP, and L-NAME groups. Endogenous effluent levels of L-ARG and L-CIT decrease after 24 h in isolated hearts, whereas perfusion of L-ARG improves cardiac performance, basal coronary flow, and vasodilator responses. In contrast, L-NAME, L-ARG, and AVP limit flow and performance but maintain a partial vasodilatory response to NP. **Sustained release of NO** may account for improved performance after L-ARG after hypothermia.

L10 ANSWER 29 OF 38 USPATFULL

AN 96:72873 USPATFULL

TI Preventing conversion of citrulline to argininosuccinate to limit pathological **nitric oxide** overproduction

IN Gross, Steven S., New York, NY, United States  
Griffith, Owen W., Milwaukee, WI, United States

PA The Medical College of Wisconsin Research Foundation, Inc., Milwaukee, WI, United States (U.S. corporation)

PI US 5545625 19960813

AI US 1994-354585 19941212 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Jordan, Kimberly

CLMN Number of Claims: 35

ECL Exemplary Claim: 1

DRWN 5 Drawing Figure(s); 5 Drawing Page(s)

LN.CNT 1146

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Administration of argininosuccinate synthetase activity reducing agents, e.g., argininosuccinate synthetase induction blocking agents (e.g., antibiotics that bind to DNA sequences present in the upstream regulatory region of the argininosuccinate synthetase gene, such as mithramycin) and argininosuccinate synthetase inhibitors (e.g., L-citrulline antagonists such as methyl citrulline and L-aspartate antagonists such as D-aspartate) is useful to prevent or treat sepsis or cytokine-induced systemic hypotension, is useful in the treatment of sepsis or cytokine-induced systemic hypotension to restore vascular sensitivity to the effects of  $\alpha$ .sub.1 -adrenergic agonists, and is useful to suppress an immune response, e.g., in treating inflammation. In one embodiment, certain argininosuccinate synthetase activity reducing agents are used together with arginine antagonists to treat sepsis or cytokine induced hypotension.

L10 ANSWER 30 OF 38 USPATFULL

AN 95:105837 USPATFULL

TI Ovulation control by regulating **nitric oxide** levels

with arginine derivatives  
IN Garfield, Robert E., Friendswood, TX, United States  
Yallampalli, Chandrasekhar, Houston, TX, United States  
PA Board of Regents, the University of Texas System, Austin, TX, United States (U.S. corporation)  
PI US 5470847 19951128  
AI US 1993-165309 19931210 (8)  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Criares, Theodore J.  
LREP Arnold, White & Durkee  
CLMN Number of Claims: 19  
ECL Exemplary Claim: 1  
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)  
LN.CNT 616

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Inhibition of ovulation in a female may be achieved by administering an arginine derivative which acts as a **nitric oxide** synthase inhibitor, alone or in combination with one or more of a progestin, an estrogen, and an LH-RH antagonist, thereby preventing conception.

L10 ANSWER 31 OF 38 USPATFULL

AN 94:99937 USPATFULL  
TI Arginine compounds as ocular hypotensive agents  
IN Varma, Rajender S., The Woodlands, TX, United States  
Chiou, George C. Y., College Station, TX, United States  
PA Baylor College of Medicine, Houston, TX, United States (U.S. corporation)  
PI US 5364884 19941115  
AI US 1993-7347 19930121 (8)  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Conrad, Joseph M.  
LREP Arnold White & Durkee  
CLMN Number of Claims: 12  
ECL Exemplary Claim: 1  
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)  
LN.CNT 1197

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to arginine and arginine-like compounds and to methods employing these compounds as ocular hypotensive agents. These compounds are effective when applied topically, may be used in low concentrations and are nontoxic. Additionally, the invention includes several new arginine derivatives with varying lipophilicities particularly suited for topical administration.

L10 ANSWER 32 OF 38 MEDLINE

AN 94194253 MEDLINE  
DN 94194253 PubMed ID: 8145021  
TI Regulation of hepatic endothelial cell and macrophage proliferation and **nitric oxide** production by GM-CSF, M-CSF, and IL-1 beta following acute endotoxemia.  
AU Feder L S; Laskin D L  
CS Department of Pharmacology and Toxicology, Rutgers University, Piscataway, New Jersey 08855-0789.  
NC ES05022 (NIEHS)  
GM34310 (NIGMS)  
SO JOURNAL OF LEUKOCYTE BIOLOGY, (1994 Apr) 55 (4) 507-13.  
Journal code: IWY; 8405628. ISSN: 0741-5400.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals

EM 199405  
ED Entered STN: 19940511  
Last Updated on STN: 19960129  
Entered Medline: 19940505  
AB Treatment of rats with bacterially derived lipopolysaccharide (LPS), a condition that mimics acute endotoxemia, results in a significant increase in the number of endothelial cells and macrophages in the liver. This is correlated with the release of proinflammatory and cytotoxic mediators that induce liver damage. In the present studies, we analyzed the effects of various inflammatory mediators released during the pathogenesis of hepatic injury on proliferation of liver nonparenchymal cells. To induce acute endotoxemia female Sprague-Dawley rats were injected intravenously with 5 mg/kg LPS. Endothelial cells and macrophages were isolated 48 h later by combined collagenase and pronase perfusion of the liver followed by centrifugal elutriation. Interleukin-1 alpha (IL-1 alpha), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-alpha) had no effect on proliferation of either endothelial cells or macrophages. In contrast, whereas interleukin-1 beta (IL-1 beta) inhibited the proliferation of endothelial cells from untreated rats, this cytokine stimulated the growth of cells from endotoxemic rats. The colony-stimulating factors, granulocyte-macrophage colony-stimulating factor (GM-CSF) and macrophage colony-stimulating factor (M-CSF), also markedly enhanced the proliferation of endothelial cells, as well as macrophages from endotoxemic rats. Macrophages from endotoxemic rats were more sensitive to the colony-stimulating factors than cells from untreated rats. In contrast, the inflammatory mediators LPS and interferon-gamma (IFN-gamma) inhibited endothelial cell and macrophage growth, an effect that was partially blocked in endothelial cells by the **nitric oxide** synthase inhibitor NG-monomethyl-L-arginine (L-NMMA). This suggests that growth inhibition in these cells is mediated, in part, by **nitric oxide**. Interestingly, in both endothelial cells and macrophages from endotoxemic rats, GM-CSF, M-CSF, and IL-1 beta synergized with LPS and IFN-gamma to induce **nitric oxide** production. This was correlated with a further inhibition of proliferation that was partially reversed by L-NMMA in endothelial cells but not macrophages. Taken together these data demonstrate that endothelial cell and macrophage proliferation in the liver is **controlled** by a variety of mediators **released** during endotoxemia; however, the mechanisms regulating growth in the two cell types are distinct.

L10 ANSWER 33 OF 38 MEDLINE  
AN 94282474 MEDLINE  
DN 94282474 PubMed ID: 8012717  
TI Prevention by insulin treatment of endothelial dysfunction but not enhanced noradrenaline-induced contractility in mesenteric resistance arteries from streptozotocin-induced diabetic rats.  
AU Taylor P D; Oon B B; Thomas C R; Poston L  
CS Division of Physiology, United Medical School Smooth Muscle Group, London.  
SO BRITISH JOURNAL OF PHARMACOLOGY, (1994 Jan) 111 (1) 35-41.  
Journal code: B00; 7502536. ISSN: 0007-1188.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199407  
ED Entered STN: 19940810  
Last Updated on STN: 19940810  
Entered Medline: 19940725  
AB 1. Streptozotocin-induced diabetic rats (Wistar) were implanted with **sustained release** insulin pellets (**release** rate = 4 u day<sup>-1</sup>) or with placebo pellets (palmitic acid) from the onset of glycosuria. 2. Noradrenaline sensitivity, **endothelium**-dependent relaxation to acetylcholine and **endothelium**-independent relaxation to sodium nitroprusside were assessed in

mesenteric resistance arteries from the insulin-treated (IT) diabetic animals and compared to placebo-implanted (PI) diabetics and age-matched controls. 3. Arteries from PI-diabetic rats (8-10 weeks) demonstrated an enhanced maximal response to noradrenaline compared to controls, which was not prevented by insulin treatment (control 2.65 +/- 0.17 mN mm-1, n = 18 arteries versus PI-diabetic 3.73 +/- 0.40 mM mm-1, n = 5, P < 0.05; control versus IT-diabetic 4.02 +/- 0.19 mN mm-1, n = 22, P < 0.001). Sensitivity to noradrenaline was similar between the three groups. 4. In the presence of the **nitric oxide** synthase inhibitor NG-nitro-L-arginine methyl ester (L-NAME), IT and PI arteries were more sensitive to noradrenaline than control arteries (pEC50: control 5.75 +/- 0.08, n = 17, versus PI-diabetic 6.14 +/- 0.09, n = 8, P < 0.05; control versus IT-diabetic 6.38 +/- 0.08, n = 20, P < 0.001). 5. The maximum contractile response to depolarizing 125 mM K+ was significantly enhanced in IT-diabetic arteries but not PI-diabetic when compared to control arteries (maximum response: control 3.74 +/- 0.15 mN mm-1, n = 18, versus PI-diabetic 3.61 +/- 0.19 mN mm-1, n = 11, NS; control versus IT-diabetic 4.66 +/- 0.18 mN mm-1, n = 22, P < 0.001). 6. **Endothelium**-dependent relaxation to acetylcholine was profoundly impaired in the PI-diabetic arteries, but in the IT-diabetic arteries was not significantly different from controls (pEC50: control 7.64 +/- 0.19, n = 17, versus PI-diabetic 6.07 +/- 0.12, n = 8, P < 0.001; control versus IT-diabetic 7.36 +/- 0.09, n = 22, NS). (ABSTRACT TRUNCATED AT 250 WORDS)

L10 ANSWER 34 OF 38 USPATFULL

AN 93:46443 USPATFULL

TI Use of L-arginine in the treatment of hypertension and other vascular disorders

IN Levere, Richard D., 5 Seymour Pl. W., Armonk, NY, United States 10504  
Abraham, Nader G., 143 Charter Cir., Ossining, NY, United States 10562  
Schwartzman, Michel L., 415 Old Country Rd., Elmsford, NY, United States 10523

Martasek, Pavel, 60 Hillcrest Rd., Hartsdale, NY, United States 10530

PI US 5217997 19930608

AI US 1992-873892 19920424 (7)

RLI Continuation of Ser. No. US 1990-513895, filed on 24 Apr 1990, now abandoned which is a continuation-in-part of Ser. No. US 1990-462638, filed on 9 Jan 1990, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Robinson, Allen J.

LREP Burns, Doane, Swecker & Mathis

CLMN Number of Claims: 19

ECL Exemplary Claim: 1

DRWN 3 Drawing Figure(s); 3 Drawing Page(s)

LN.CNT 645

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for treating a high vascular resistance disorder in a mammal by administering to a mammalian organism in need of such treatment a sufficient amount of L-arginine or pharmaceutically acceptable salt thereof to treat a high vascular resistance disorder. The L-arginine is typically administered in the range of about 1 mg to 1500 mg per day. High vascular resistance disorders include hypertension, primary or secondary vasospasm, angina pectoris, cerebral ischemia and preeclampsia. Also disclosed is a method for preventing or treating bronchial asthma in a mammal by administering to a mammalian organism in need of such prevention or treatment a sufficient amount of L-arginine to prevent or treat bronchial asthma.

L10 ANSWER 35 OF 38 MEDLINE

AN 92216787 MEDLINE

DN 92216787 PubMed ID: 1373103

TI Different patterns of release of **endothelium**-derived relaxing factor and prostacyclin.

AU Mitchell J A; de Nucci G; Warner T D; Vane J R  
CS William Harvey Research Institute, Saint Bartholomew's Hospital Medical College, London.  
SO BRITISH JOURNAL OF PHARMACOLOGY, (1992 Feb) 105 (2) 485-9.  
Journal code: B00; 7502536. ISSN: 0007-1188.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199205  
ED Entered STN: 19920529  
Last Updated on STN: 19960129  
Entered Medline: 19920508

AB 1. Release of **endothelium** derived relaxing factor (EDRF) and prostacyclin (PGI2) from endothelial cells (EC) cultured from bovine aortae was measured by bioassay and radioimmunoassay, respectively, during infusions (10 min) of bradykinin (BK), adenosine diphosphate (ADP), arachidonic acid (AA), alkaline buffers and the free-bases (FB) of L-arginine or D-arginine. Release of EDRF from the lumenally perfused rabbit aorta was also measured during infusions (10 min) of acetylcholine (ACh), substance P and ADP. 2. Bradykinin (10 or 30 nM) infused through the column of EC induced release of both EDRF and PGI2, neither of which was maintained for the duration of the infusion. 3. ADP (1.6 or 4 microM) infused through the column of EC induced release of a EDRF which was maintained for the duration of the infusion and a release of PGI2 which lasted for a much shorter period. 4. Arachidonic acid (30 or 90 microM) infused through the column of EC caused a **sustained release** of EDRF and PGI2, both of which outlasted the infusion of AA. 5. L-Arginine FB, D-arginine FB or alkaline buffer infused through the column of EC released EDRF, but only small amounts of PGI2. The release of EDRF outlasted the period of infusion and was due to an increase in the pH of the Krebs solution perfusing the EC. 6. Infusions of ACh (0.25-1 microM) or ADP (4-16 microM) caused a **sustained release** of EDRF from the lumenally-perfused rabbit aorta, whereas infusion of substance P (3.3-10 microM) caused only a transient release of EDRF. 7. These results show that distinct patterns of EDRF release exist to different agonists in both cultured and in situ EC, and that EDRF and PGI2 do not necessarily follow the same time course of **release**. Furthermore, **sustained release** of EDRF does not require the constant infusion of the precursor, L-arginine, whereas **sustained release** of PGI2 only occurs when AA, the precursor of PGI2, is present in the extracellular medium.

L10 ANSWER 36 OF 38 MEDLINE  
AN 93164523 MEDLINE  
DN 93164523 PubMed ID: 1287271  
TI Involvement of **nitric oxide** in **endothelium**  
-dependent, phasic relaxation caused by histamine in monkey cerebral arteries.

AU Ayajiki K; Okamura T; Toda N  
CS Department of Pharmacology, Shiga University of Medical Sciences, Ohtsu, Japan.  
SO JAPANESE JOURNAL OF PHARMACOLOGY, (1992 Dec) 60 (4) 357-62.  
Journal code: KO7; 2983305R. ISSN: 0021-5198.  
CY Japan  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199303  
ED Entered STN: 19930402  
Last Updated on STN: 19970203  
Entered Medline: 19930317

AB Monkey cerebral artery strips partially contracted with prostaglandin F2 alpha responded to histamine with biphasic patterns of relaxation. The

delayed and sustained relaxation was suppressed by cimetidine, whereas the phasic response was abolished by treatment with chlorpheniramine and NG-nitro-L-arginine (L-NA), a **nitric oxide (NO)** synthase inhibitor. The inhibition by L-NA was reversed by L-arginine. D-NA was without effect. **Endothelium** denudation abolished the phasic relaxation. We hypothesized that **endothelium**-dependent, phasic relaxations caused by histamine are mediated by **NO** that is **released** by H1-receptor stimulation, whereas the **sustained** relaxation is associated with the activation of H2-receptors in the smooth muscle of monkey cerebral arteries.

L10 ANSWER 37 OF 38 MEDLINE  
 AN 93060391 MEDLINE  
 DN 93060391 PubMed ID: 1434097  
 TI Nitroarginine-sensitive and -insensitive components of the **endothelium**-dependent relaxation in the guinea-pig carotid artery.  
 AU Suzuki H; Chen G; Yamamoto Y; Miwa K  
 CS Department of Physiology, Nagoya City University Medical School, Japan.  
 SO JAPANESE JOURNAL OF PHYSIOLOGY, (1992) 42 (2) 335-47.  
 Journal code: KON; 2985184R. ISSN: 0021-521X.  
 CY Japan  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199212  
 ED Entered STN: 19930122  
 Last Updated on STN: 19970203  
 Entered Medline: 19921203  
 AB In the guinea-pig carotid arteries, nitroarginine elevated the resting tension (greater than  $3 \times 10^{-6}$  M) and enhanced the noradrenaline (NA)- and high-potassium (high-K, 29.6 mM) induced contractions (greater than  $10^{-7}$  M), in a concentration-dependent manner, with **no** significant change in the resting membrane potential and depolarizations elicited by NA or high-K. ACh ( $10^{-6}$  M) relaxed the muscles precontracted with NA or high-K by 96 or 46% of the contraction, respectively. In the presence of nitroarginine ( $10^{-5}$  M) for 1-3 h, the ACh-induced relaxation was reduced to 40 or 0% of the NA- or high-K-contractions, respectively. In tissues contracted with NA and exposed to nitroarginine, the ACh-induced relaxation changed from a sustained to a transient form. ACh relaxed the muscles to a similar extent, at any given level of tension, as elevated by different concentrations of NA to 1-3 times the level produced by  $10^{-6}$  M NA, either in the presence or absence of nitroarginine. ACh (greater than  $10^{-8}$  M) produced a transient hyperpolarization of the membrane, in an **endothelium**-dependent manner, and the responses were blocked by atropine ( $10^{-6}$  M) or high-K solution, but not by NA or nitroarginine. We propose that 1) **endothelium**-derived hyperpolarizing factor (EDHF) is produced by pathways independent of the biosynthesis of **endothelium**-derived relaxing factor (EDRF), 2) the **sustained release** of EDRF maintains the muscle tone at a low level, and 3) the **endothelium**-dependent relaxation is produced by both EDRF and EDHF, and they elicit sustained and transient relaxations, respectively.

L10 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
 AN 1990:529813 CAPLUS  
 DN 113:129813  
 TI Cultured endothelial cells maintain their L-arginine level despite the continuous release of EDRF  
 AU Mitchell, Jane A.; Hecker, Markus; Anggard, Erik E.; Vane, John R.  
 CS Med. Coll., St. Bartholomew's Hosp., London, EC1M 6BQ, UK  
 SO Eur. J. Pharmacol. (1990), 182(3), 573-6  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 DT Journal  
 LA English

AB Endothelial cells cultured from bovine aorta and grown on microcarrier beads contain 107  $\mu\text{M}$  L-arginine (Arg). When packed into a jacketed chromatog. column and perfused with Krebs soln., the cells showed a substantial and **sustained release** of **endothelium**-derived relaxing factor (EDRF) for  $\geq 2$  h, which was further enhanced by infusions of ADP (4  $\mu\text{M}$ ). In contrast to other amino acids, such as L-alanine, L-aspartate, L-glutamine, L-glutamate, or L-serine, which showed a time-dependent decrease to <30% of their original level within 2 h, Arg remained at control levels for 30 min and decreased only by 25% after 2 h. Thus, endothelial cells can generate Arg from an intracellular source to maintain their Arg level despite the continuous formation of EDRF.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 15:51:18 ON 23 MAR 2002

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COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	0.15	0.15

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DICTIONARY FILE UPDATES: 20 MAR 2002 HIGHEST RN 402467-99-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when  
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for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

The P indicator for Preparations was not generated for all of the  
CAS Registry Numbers that were added to the H/Z/CA/CAPLUS files between  
12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches  
during this period, either directly appended to a CAS Registry Number  
or by qualifying an L-number with /P, may have yielded incomplete results.  
As of 1/23/02, the situation has been resolved. Also, note that searches  
conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAPLUS files  
incorporating CAS Registry Numbers with the P indicator between 12/27/01  
and 1/23/02, are encouraged to re-run these strategies. Contact the  
CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698,  
worldwide, or send an e-mail to [help@cas.org](mailto:help@cas.org) for further assistance or to  
receive a credit for any duplicate searches.

=> e arginine/cn

E1	1	ARGININANILIDE, N.ALPHA.,N.OMEGA.,N.OMEGA.-TRIS(PHENYLCARBAM OYL)-, L-/CN
E2	1	ARGININANILIDE, N2-BENZOYL-/CN
E3	2 -->	ARGININE/CN
E4	1	ARGININE .BETA.-NAPHTHYLAMIDE/CN
E5	1	ARGININE 2,2,2-TRICHLOROETHYL ESTER/CN
E6	1	ARGININE 2-MONOOXYGENASE/CN
E7	1	ARGININE 3RD TRANSPORT SYSTEM PERIPLASMIC BINDING PROTEIN (E SCHERICHIA COLI O157:H7 STRAIN EDL933 GENE ARTI)/CN
E8	1	ARGININE 3RD TRANSPORT SYSTEM PERIPLASMIC BINDING PROTEIN (E SCHERICHIA COLI O157:H7 STRAIN EDL933 GENE ARTJ)/CN
E9	1	ARGININE 3RD TRANSPORT SYSTEM PERIPLASMIC BINDING PROTEIN (E SCHERICHIA COLI STRAIN O157:H7 GENE ECS0943)/CN
E10	1	ARGININE 3RD TRANSPORT SYSTEM PERIPLASMIC BINDING PROTEIN (E SCHERICHIA COLI STRAIN O157:H7 GENE ECS0946)/CN
E11	1	ARGININE 3RD TRANSPORT SYSTEM PERMEASE PROTEIN (ESCHERICHIA

COLI O157:H7 STRAIN EDL933 GENE ARTM)/CN  
E12 1 ARGININE 3RD TRANSPORT SYSTEM PERMEASE PROTEIN (ESCHERICHIA  
COLI O157:H7 STRAIN EDL933 GENE ARTQ)/CN

=> s e3

L1 2 ARGININE/CN

=> d l1

L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2002 ACS

RN 7200-25-1 REGISTRY

CN **Arginine (9CI)** (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Arginine, DL- (8CI)

CN DL-Arginine

OTHER NAMES:

CN (.+-.)-Arginine

FS 3D CONCORD

MF C6 H14 N4 O2

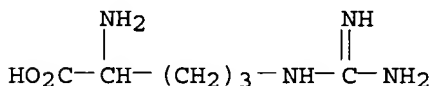
CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
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269 REFERENCES IN FILE CA (1967 TO DATE)

13 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

269 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus, uspatfull, biosis, medline, wpids, drugu, scisearch

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SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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=> s l1

'CN' IS NOT A VALID FIELD CODE

L2 73808 L1

=> s arginin

L3 573 ARGININ

=> s arginin###

L4 294956 ARGININ###

=> s l4 orl2

MISSING OPERATOR L4 ORL2

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s l4 or l2

L5 298505 L4 OR L2

=> s controlled(3a)release#####

L6 60495 CONTROLLED(3A) RELEASE#####

=> s controlled(5a)release#####

L7 65680 CONTROLLED(5A) RELEASE#####

=> s sustained(5a)release#####

L8 56524 SUSTAINED(5A) RELEASE#####

=> s extended(5a)release#####

L9 10475 EXTENDED(5A) RELEASE#####

=> s time-programmed(5a)releas#####

L10 14 TIME-PROGRAMMED(5A) RELEAS#####

=> s l10 or l9 or l8 or l7

L11 121314 L10 OR L9 OR L8 OR L7

=> s l11 and l5

L12 4501 L11 AND L5

=> s matrix

L13 1131261 MATRIX

=> s l13 and l12

L14 1927 L13 AND L12

=> s nitric oxid## or NO

L15 7451330 NITRIC OXID## OR NO

=> s l13 and l11

L16 19806 L13 AND L11

=> s l5 and l15

L17 111519 L5 AND L15

=> s l17 and l16

L18 142 L17 AND L16

=> s vasodilat####

L19 220656 VASODILAT####

=> s vascula###(5a)(NO or nitric oxide#)  
L20 25210 VASCULA###(5A)(NO OR NITRIC OXIDE#)

=> s 15 and 120  
L21 5856 L5 AND L20

=> s 15 and 119  
L22 18258 L5 AND L19

=> s 116 and 121  
L23 29 L16 AND L21

=> s 116 and 122  
L24 176 L16 AND L22

=> s 115 and 124  
L25 71 L15 AND L24

=> dup remove 123  
PROCESSING COMPLETED FOR L23  
L26 29 DUP REMOVE L23 (0 DUPLICATES REMOVED)

=> dup remove 125  
PROCESSING COMPLETED FOR L25  
L27 71 DUP REMOVE L25 (0 DUPLICATES REMOVED)

=> s endothelium(6a)relaxat#####  
L28 19115 ENDOTHELIUM(6A) RELAXAT#####

=> s 127 and 128  
L29 17 L27 AND L28

=> s 128 and 126  
L30 11 L28 AND L26

=> d 129 1-17 bib,ab

L29 ANSWER 1 OF 17 USPATFULL  
AN 2002:48258 USPATFULL  
TI 26 Human secreted proteins  
IN Ruben, Steven M., Olney, MD, UNITED STATES  
Birse, Charles E., North Potomac, MD, UNITED STATES  
Duan, Roxanne D., Bethesda, MD, UNITED STATES  
Soppet, Daniel R., Centreville, VA, UNITED STATES  
Rosen, Craig A., Laytonsville, MD, UNITED STATES  
Shi, Yanggu, Gaithersburg, MD, UNITED STATES  
LaFleur, David W., Washington, DC, UNITED STATES  
Olsen, Henrik, Gaithersburg, MD, UNITED STATES  
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES  
Florence, Kimberly A., Rockville, MD, UNITED STATES  
Ni, Jian, Rockville, MD, UNITED STATES  
Young, Paul, Gaithersburg, MD, UNITED STATES  
PI US 2002028449 A1 20020307  
AI US 2000-726643 A1 20001201 (9)  
RLI Continuation-in-part of Ser. No. WO 2000-US15187, filed on 2 Jun 2000,  
UNKNOWN  
PRAI US 1999-137725P 19990607 (60)  
DT Utility  
FS APPLICATION  
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850  
CLMN Number of Claims: 23  
ECL Exemplary Claim: 1  
DRWN No Drawings

LN.CNT 20287

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

L29 ANSWER 2 OF 17 USPATFULL

AN 2002:43671 USPATFULL

TI 49 human secreted proteins

IN Moore, Paul A., Germantown, MD, UNITED STATES  
Ruben, Steven M., Olney, MD, UNITED STATES  
Olsen, Henrik S., Gaithersburg, MD, UNITED STATES  
Shi, Yanggu, Gaithersburg, MD, UNITED STATES  
Rosen, Craig A., Laytonsville, MD, UNITED STATES  
Florence, Kimberly A., Rockville, MD, UNITED STATES  
Soppet, Daniel R., Centreville, VA, UNITED STATES  
LaFleur, David W., Washington, DC, UNITED STATES  
Endress, Gregory A., Potomac, MD, UNITED STATES  
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES  
Komatsoulis, George, Silver Spring, MD, UNITED STATES  
Duan, Roxanne D., Bethesda, MD, UNITED STATES

PI US 2002026040 A1 20020228

AI US 2001-904615 A1 20010716 (9) \

RLI Continuation of Ser. No. US 2000-739254, filed on 19 Dec 2000, PENDING  
Continuation of Ser. No. US 2000-511554, filed on 23 Feb 2000, ABANDONED  
Continuation-in-part of Ser. No. WO 1999-US19330, filed on 24 Aug 1999,  
UNKNOWN

PRAI US 1998-97917P 19980825 (60)

US 1998-98634P 19980831 (60)

DT Utility

FS APPLICATION

LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 19401

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

L29 ANSWER 3 OF 17 USPATFULL

AN 2002:43668 USPATFULL

TI VASCULAR ENDOTHELIAL GROWTH FACTOR 3 ANTIBODIES

IN HU, JING-SHAN, SUNNYVALE, CA, UNITED STATES  
OLSEN, HENRIK, GAITHERSBURG, MD, UNITED STATES  
ROSEN, CRAIG A., LAYTONSVILLE, MD, UNITED STATES

PI US 2002026037 A1 20020228

AI US 1999-244694 A1 19990210 (9)

RLI Continuation-in-part of Ser. No. US 1998-132088, filed on 10 Aug 1998,  
ABANDONED Continuation-in-part of Ser. No. US 1998-33662, filed on 3 Mar  
1998, PENDING Division of Ser. No. US 1995-469641, filed on 6 Jun 1995,  
PENDING

DT Utility

FS APPLICATION

LREP STERNE KESSLER GOLDSTEIN & FOX, 1100 NEW YORK AVENUE N W, SUITE 600,  
WASHINGTON, DC, 200053934

CLMN Number of Claims: 25  
ECL Exemplary Claim: 1  
DRWN 5 Drawing Page(s)  
LN.CNT 6301

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a novel human protein called Vascular Endothelial Growth Factor 3, and isolated polynucleotides encoding this protein. Also provided are vectors, host cells, antibodies, and recombinant methods for producing this human protein. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to this novel human protein.

L29 ANSWER 4 OF 17 USPATFULL

AN 2002:43187 USPATFULL

TI Transforming growth factor alpha HIII

IN Wei, Ying-Fei, Berkeley, CA, UNITED STATES

PI US 2002025553 A1 20020228

AI US 2000-726348 A1 20001201 (9)

RLI Continuation-in-part of Ser. No. US 1997-778545, filed on 3 Jan 1997, PENDING

PRAI US 1996-11136P 19960104 (60)

US 1999-168387P 19991202 (60)

DT Utility

FS APPLICATION

LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850

CLMN Number of Claims: 25

ECL Exemplary Claim: 1

DRWN 5 Drawing Page(s)

LN.CNT 11810

AB The present invention relates to a novel human protein called Transforming Growth Factor Alpha III, and isolated polynucleotides encoding this protein. Also provided are vectors, host cells, antibodies, and recombinant methods for producing this human protein. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to this novel human protein.

L29 ANSWER 5 OF 17 USPATFULL

AN 2002:30030 USPATFULL

TI Electrically induced vessel **vasodilation**

IN Dev, Nagendu B., San Diego, CA, United States

Dev, Sukhendu B., San Diego, CA, United States

Hofmann, Gunter A., San Diego, CA, United States

PA Genetronics Inc., San Diego, CA, United States (U.S. corporation)

PI US 6347247 B1 20020212

AI US 1999-307216 19990507 (9)

PRAI US 1998-84857P 19980508 (60)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Evanisko, George R.

LREP Gray Cary Ware & Freidenrich LLP, Haile, Lisa A.

CLMN Number of Claims: 12

ECL Exemplary Claim: 1

DRWN 8 Drawing Figure(s); 8 Drawing Page(s)

LN.CNT 1421

AB The invention provides methods for inducing or increasing the **vasodilation** of a vessel. The invention further provides methods for inducing or increasing the flow of fluid through a vessel. An electrical impulse is applied to the vessel in order to induce or increase vessel **vasodilation** or to induce or increase the flow of fluid through the vessel. In a particular embodiment, a novel double-balloon catheter system incorporating electroporation technology has been designed and is used to apply the electrical impulse endoluminally.

L29 ANSWER 6 OF 17 USPATFULL

AN 2002:27766 USPATFULL

TI Electrically induced vessel **vasodilation**

IN Dev, Nagendu B., San Diego, CA, UNITED STATES  
Dev, Sukhendu B., San Diego, CA, UNITED STATES  
Hofmann, Gunter A., San Diego, CA, UNITED STATES

PI US 2002016615 A1 20020207

AI US 2001-969367 A1 20011001 (9)

RLI Continuation of Ser. No. US 1999-307216, filed on 7 May 1999, PENDING

PRAI US 1998-84857P 19980508 (60)

DT Utility

FS APPLICATION

LREP GARY CARY WARE & FRIENDENRICH LLP, 4365 EXECUTIVE DRIVE, SUITE 1600, SAN  
DIEGO, CA, 92121-2189

CLMN Number of Claims: 21

ECL Exemplary Claim: 1

DRWN 8 Drawing Page(s)

LN.CNT 1464

AB The invention provides methods for inducing or increasing the **vasodilation** of a vessel. The invention further provides methods for inducing or increasing the flow of fluid through a vessel. An electrical impulse is applied to the vessel in order to induce or increase vessel **vasodilation** or to induce or increase the flow of fluid through the vessel. In a particular embodiment, a novel double-balloon catheter system incorporating electroporation technology has been designed and is used to apply the electrical impulse endoluminally.

L29 ANSWER 7 OF 17 USPATFULL

AN 2002:22131 USPATFULL

TI 18 Human secreted proteins

IN Shi, Yanggu, Gaithersburg, MD, UNITED STATES  
Young, Paul E., Gaithersburg, MD, UNITED STATES  
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES  
Soppet, Daniel R., Centreville, VA, UNITED STATES  
Ruben, Steven M., Olney, MD, UNITED STATES

PI US 2002012966 A1 20020131

AI US 2001-768826 A1 20010125 (9)

RLI Continuation-in-part of Ser. No. WO 2000-US22350, filed on 15 Aug 2000, UNKNOWN

PRAI US 1999-148759P 19990816 (60)

DT Utility

FS APPLICATION

LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 18157

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

L29 ANSWER 8 OF 17 USPATFULL

AN 2001:202682 USPATFULL

TI Therapeutic methods employing disulfide derivatives of dithiocarbonates and compositions useful therefor

IN Lai, Ching-San, Encinitas, CA, United States  
Vassilev, Vassil, San Diego, CA, United States

PA Medinox, Inc., San Diego, CA, United States (U.S. corporation)  
PI US 6316502 B1 20011113  
AI US 2000-565666 20000505 (9)  
RLI Division of Ser. No. US 1998-103639, filed on 23 Jun 1998, now patented,  
Pat. No. US 6093743  
DT Utility  
FS GRANTED  
EXNAM Primary Examiner: Weddington, Kevin E.  
LREP Reiter, Stephen E.Foley & Lardner  
CLMN Number of Claims: 14  
ECL Exemplary Claim: 1  
DRWN 11 Drawing Figure(s); 5 Drawing Page(s)  
LN.CNT 2591

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a novel dithiocarbamate disulfide dimer useful in various therapeutic treatments, either alone or in combination with other active agents. In one method, the disulfide derivative of a dithiocarbamate is coadministered with an agent that inactivates (or inhibits the production of) species that induce the expression of **nitric oxide** synthase to reduce the production of such species, while, at the same time reducing **nitric oxide** levels in the subject. In another embodiment, free iron ion levels are reduced in a subject by administration of a disulfide derivative of a dithiocarbamate(s) to scavenge free iron ions, for example, in subjects undergoing anthracycline chemotherapy. In another embodiment, cyanide levels are reduced in a subject by administration of a disulfide derivative of a dithiocarbamate so as to bind cyanide in the subject. In a further aspect, the present invention relates to compositions and formulations useful in such therapeutic methods.

L29 ANSWER 9 OF 17 USPATFULL

AN 2001:179068 USPATFULL  
TI Heart homing peptides and methods of using same  
IN Ruoslahti, Erkki, Rancho Santa Fe, CA, United States  
MacKenna, Deidre A., San Diego, CA, United States  
PA The Burnham Institute, La Jolla, CA, United States (U.S. corporation)  
PI US 6303573 B1 20011016  
AI US 1999-326718 19990607 (9)  
DT Utility  
FS GRANTED  
EXNAM Primary Examiner: Davenport, Avis M.  
LREP Campbell & Flores LLP  
CLMN Number of Claims: 27  
ECL Exemplary Claim: 1  
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)  
LN.CNT 1532

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a heart homing peptide that contains the amino acid sequence GGGVFWQ (SEQ ID NO: 2); HGRVRPH (SEQ ID NO: 3); VVLVTSS (SEQ ID NO: 4); CLHRGNSC (SEQ ID NO: 9); or CRSWNKADNRSC (SEQ ID NO: 10) and further provides conjugates in which a heart homing peptide is linked to a moiety such as a therapeutic agent. The conjugates of the invention are useful for treating cardiovascular diseases such as atherosclerosis and restenosis.

L29 ANSWER 10 OF 17 USPATFULL

AN 2001:155766 USPATFULL  
TI 49 human secreted proteins  
IN Moore, Paul A., Germantown, MD, United States  
Ruben, Steven M., Oley, MD, United States  
Olsen, Henrik S., Gaithersburg, MD, United States  
Shi, Yanggu, Gaithersburg, MD, United States  
Rosen, Craig A., Laytonsville, MD, United States  
Florence, Kimberly A., Rockville, MD, United States

Soppet, Daniel R., Centreville, VA, United States  
Lafleur, David W., Washington, DC, United States  
Endress, Gregory A., Potomac, MD, United States  
Ebner, Reinhard, Gaithersburg, MD, United States  
Komatsoulis, George, Silver Spring, MD, United States  
Duan, Roxanne D., Bethesda, MD, United States

PI US 2001021700 A1 20010913  
AI US 2000-739254 A1 20001219 (9)  
RLI Continuation of Ser. No. US 2000-511554, filed on 23 Feb 2000, ABANDONED  
Continuation-in-part of Ser. No. WO 1999-US19330, filed on 24 Aug 1999,  
UNKNOWN  
PRAI US 1998-97917P 19980825 (60)  
US 1998-98634P 19980831 (60)  
DT Utility  
FS APPLICATION  
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850  
CLMN Number of Claims: 23  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 15462

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

L29 ANSWER 11 OF 17 USPATFULL

AN 2001:139293 USPATFULL  
TI Fibroblast growth factor receptor-5  
IN Young, Paul E., Gaithersburg, MD, United States  
Ruben, Steven M., Olney, MD, United States  
PI US 2001016335 A1 20010823  
AI US 2001-758386 A1 20010112 (9)  
RLI Continuation of Ser. No. US 1999-293182, filed on 16 Apr 1999, ABANDONED  
PRAI US 1998-105465P 19981023 (60)  
DT Utility  
FS APPLICATION  
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850  
CLMN Number of Claims: 23  
ECL Exemplary Claim: 1  
DRWN 10 Drawing Page(s)  
LN.CNT 6097

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to fibroblast growth factor receptor-5, a novel member of the fibroblast growth factor receptor family. The invention provides isolated nucleic acid molecules encoding human FGFR5 receptors. FGFR5 polypeptides are also provided, as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of FGFR5 receptor activity. Also provided are diagnostic methods for detecting disease states related to the aberrant expression of FGFR5 receptors. Further provided are therapeutic methods for treating disease states including, but not limited to, defects in wound healing, mucositis, defects in angiogenesis, ischemia, host defense dysfunction, endocrine dysfunction, disorders in immune function, and/or disorders in insulin secretion.

L29 ANSWER 12 OF 17 USPATFULL

AN 2001:111865 USPATFULL  
TI Chitosan-based **nitric oxide** donor compositions  
IN Smith, Daniel J., Stow, OH, United States

Serhatkulu, Sibel, Akron, OH, United States  
PA The University of Akron, Akron, OH, United States (U.S. corporation)  
PI US 6261594 B1 20010717  
AI US 1998-199732 19981125 (9)  
DT Utility  
FS GRANTED  
EXNAM Primary Examiner: Kulkosky, Peter F.  
LREP Renner, Kenner, Greive, Bobak, Taylor & Weber  
CLMN Number of Claims: 19  
ECL Exemplary Claim: 1  
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)  
LN.CNT 689

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A chitosan-based polymeric **nitric oxide** donor composition comprising a modified chitosan polymer and a **nitric oxide** [N2O2] dimer, wherein the **nitric oxide** [N2O2] dimer is bonded directly to the backbone of the modified chitosan polymer without further binding through a nucleophile residue or moiety. The chitosan-based polymeric **nitric oxide** donor composition is capable of site specific delivery and **controlled release of nitric oxide** under physiological conditions. The chitosan-based polymeric **nitric oxide** donor composition further provides a carrier having medically beneficial properties. A method is further included for preparing a chitosan-based polymeric **nitric oxide** donor composition comprising reacting a **nitric oxide** dimer (80-100 p.s.i.) with a modified chitosan polymer in the presence of sodium methoxide at room temperature. The chitosan-based polymeric **nitric oxide** composition can be incorporated into dry powder inhalers, wound dressings, implants, injectables, condoms, wound dressings and prosthesis coatings for use in a variety of medical applications in which an effective dosage of **nitric oxide** is indicated as a preferred method of treatment.

L29 ANSWER 13 OF 17 USPATFULL

AN 2001:14453 USPATFULL

TI Upregulation of Type III endothelial cell **nitric oxide** synthase by rho GTPase function inhibitors

IN Liao, James K., Weston, MA, United States

PA Brigham and Women's Hospital, Inc., Boston, MA, United States (U.S. corporation)

PI US 6180597 B1 20010130

AI US 1998-132849 19980811 (9)

RLI Continuation-in-part of Ser. No. US 1998-92618, filed on 5 Jun 1998, now abandoned

PRAI US 1998-78774P 19980319 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Russell, Jeffrey E.

LREP Wolf, Greenfield & Sacks, P.C.

CLMN Number of Claims: 93

ECL Exemplary Claim: 1

DRWN 27 Drawing Figure(s); 16 Drawing Page(s)

LN.CNT 2725

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A use for rho GTPase function inhibitors is provided. In the instant invention, rho GTPase function inhibitors are found to upregulate endothelial cell **Nitric Oxide** Synthase activity. As a result, rho GTPase function inhibitors are useful in treating or preventing conditions that result from the abnormally low expression and/or activity of endothelial cell **Nitric Oxide** Synthase. Such conditions include pulmonary hypertension, ischemic stroke, impotence, heart failure, hypoxia-induced conditions, insulin deficiency, progressive renal disease, gastric or esophageal motility

syndrome, etc. Subjects thought to benefit mostly from such treatments include nonhyperlipidemics and nonhypercholesterolemics, but do not necessarily exclude hyperlipidemics and hypercholesterolemics.

L29 ANSWER 14 OF 17 USPATFULL

AN 2000:153742 USPATFULL

TI Upregulation of Type III endothelial cell **Nitric Oxide**  
Synthase by HMG-CoA reductase inhibitors

IN Liao, James K., Weston, MA, United States

Laufs, Ulrich, Cologne, Germany, Federal Republic of

Endres, Matthias, Berlin, Germany, Federal Republic of

Moskowitz, Michael A., Belmont, MA, United States

PA The General Hospital Corporation, Boston, MA, United States (U.S.  
corporation)

The Brigham and Women's Hospital Inc., Boston, MA, United States (U.S.  
corporation)

PI US 6147109 20001114

AI US 1998-132848 19980811 (9)

PRAI US 1997-62093P 19971014 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Jordan, Kimberly

LREP Wolf, Greenfield & Sacks, P.C.

CLMN Number of Claims: 54

ECL Exemplary Claim: 1

DRWN 18 Drawing Figure(s); 10 Drawing Page(s)

LN.CNT 1864

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A new use for HMG-CoA reductase inhibitors is provided. In the instant invention, HMG-CoA reductase inhibitors are found to upregulate endothelial cell **Nitric Oxide** Synthase activity through a mechanism other than preventing the formation of oxidative-LDL. As a result, HMG-CoA reductase inhibitors are useful in treating or preventing conditions that result from the abnormally low expression and/or activity of endothelial cell **Nitric Oxide** Synthase. Such conditions include pulmonary hypertension, ischemic stroke, impotence, heart failure, hypoxia-induced conditions, insulin deficiency, progressive renal disease, gastric or esophageal motility syndrome, etc. Subjects thought to benefit mostly from such treatments include nonhyperlipidemics and nonhypercholesterolemics, but not necessarily exclude hyperlipidemics and hypercholesterolemics.

L29 ANSWER 15 OF 17 USPATFULL

AN 2000:95042 USPATFULL

TI Therapeutic methods employing disulfide derivatives of dithiocarbamates and compositions useful therefor

IN Lai, Ching-San, Encinitas, CA, United States

Vassilev, Vassil, San Diego, CA, United States

PA Medinox Inc., San Diego, CA, United States (U.S. corporation)

PI US 6093743 20000725

AI US 1998-103639 19980623 (9)

DT Utility

FS Granted

EXNAM Primary Examiner: Weddington, Kevin E.

LREP Gary Cary Ware & Freidenrich, Reiter, Stephen E., Kirschenbaum, Shelia R.

CLMN Number of Claims: 51

ECL Exemplary Claim: 1

DRWN 11 Drawing Figure(s); 5 Drawing Page(s)

LN.CNT 2691

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a novel dithiocarbamate disulfide dimer useful in various therapeutic treatments, either alone or in combination with other active agents. In one method, the disulfide derivative of a

dithiocarbamate is coadministered with an agent that inactivates (or inhibits the production of) species that induce the expression of **nitric oxide** synthase to reduce the production of such species, while, at the same time reducing **nitric oxide** levels in the subject. In another embodiment, free iron ion levels are reduced in a subject by administration of a disulfide derivative of a dithiocarbamate(s) to scavenge free iron ions, for example, in subjects undergoing anthracycline chemotherapy. In another embodiment, cyanide levels are reduced in a subject by administration of a disulfide derivative of a dithiocarbamate so as to bind cyanide in the subject. In a further aspect, the present invention relates to compositions and formulations useful in such therapeutic methods.

L29 ANSWER 16 OF 17 USPATFULL

AN 2000:70640 USPATFULL

TI Antikinin compounds and uses thereof

IN Margolius, Harry S., Mt. Pleasant, SC, United States

PA MUSC Foundation for Research Development, Charleston, SC, United States (U.S. corporation)

PI US 6071710 20000606

AI US 1997-974735 19971119 (8)

PRAI US 1996-31285P 19961120 (60)

US 1997-64792P 19971110 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Kemmerer, Elizabeth; Assistant Examiner: Basi, Nirmal S.

LREP Needle & Rosenberg, P.C.

CLMN Number of Claims: 11

ECL Exemplary Claim: 1

DRWN 21 Drawing Figure(s); 12 Drawing Page(s)

LN.CNT 1572

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An analog of the peptide consisting of RPPGF (SEQ ID NO:1) is provided. Mimetics of RPPGF (SEQ ID NO:1) and its retropeptide, FGPPR, are also provided. A peptide is provided having an antikinin activity and having the sequence X.sub.1 -R-P-P-G-F-X.sub.2 (SEQ ID NO:5), X.sub.1 -F-G-P-P-R-X.sub.2 (SEQ ID NO:7). Provided are methods of screening for a mimetic or analog of RPPGF (SEQ ID NO:1) or FGPPR (SEQ ID NO:2), screening for an RPPGF (SEQ ID NO:1) receptor, or screening for an antagonist of RPPGF (SEQ ID NO:1) or FGPPR (SEQ ID NO:2) is provided. Methods of treating conditions that can be treated by an antikinin activity and diseases that are associated with an antikinin activity are also provided.

L29 ANSWER 17 OF 17 USPATFULL

AN 97:91551 USPATFULL

TI Amidine derivatives useful as platelet aggregation inhibitors and **vasodilators**

IN Currie, Mark G., St. Charles, MO, United States

Tjoeng, Foe S., Manchester, MO, United States

Zupec, Mark E., O'Fallon, IL, United States

PA G.D. Searle & Co., Chicago, IL, United States (U.S. corporation)

PI US 5674894 19971007

AI US 1995-440804 19950515 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Wong, King Lit

LREP Bennett, D. A.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 715

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The current invention discloses novel amidine derivatives with  
**nitric oxide** donating property that can inhibit  
platelet aggregation and promote **vasodilation** in a single  
compound.

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(FILE 'HOME' ENTERED AT 15:51:18 ON 23 MAR 2002)

FILE 'REGISTRY' ENTERED AT 15:51:29 ON 23 MAR 2002

E ARGININE/CN

L1 2 S E3

FILE 'CAPLUS, USPATFULL, BIOSIS, MEDLINE, WPIDS, DRUGU, SCISEARCH'  
ENTERED AT 15:52:30 ON 23 MAR 2002

L2 73808 S L1  
L3 573 S ARGININ  
L4 294956 S ARGININ###  
L5 298505 S L4 OR L2  
L6 60495 S CONTROLLED(3A)RELEASE#####  
L7 65680 S CONTROLLED(5A)RELEASE#####  
L8 56524 S SUSTAINED(5A)RELEASE#####  
L9 10475 S EXTENDED(5A)RELEASE#####  
L10 14 S TIME-PROGRAMMED(5A)RELEAS#####  
L11 121314 S L10 OR L9 OR L8 OR L7  
L12 4501 S L11 AND L5  
L13 1131261 S MATRIX  
L14 1927 S L13 AND L12  
L15 7451330 S NITRIC OXID## OR NO  
L16 19806 S L13 AND L11  
L17 111519 S L5 AND L15  
L18 142 S L17 AND L16  
L19 220656 S VASODILAT####  
L20 25210 S VASCULA###(5A)(NO OR NITRIC OXIDE#)  
L21 5856 S L5 AND L20  
L22 18258 S L5 AND L19  
L23 29 S L16 AND L21  
L24 176 S L16 AND L22  
L25 71 S L15 AND L24  
L26 29 DUP REMOVE L23 (0 DUPLICATES REMOVED)  
L27 71 DUP REMOVE L25 (0 DUPLICATES REMOVED)  
L28 19115 S ENDOTHELIUM(6A)RELAXAT#####  
L29 17 S L27 AND L28  
L30 11 S L28 AND L26

=> d l30 1-11 bib,ab

L30 ANSWER 1 OF 11 USPATFULL

AN 2002:48258 USPATFULL

TI 26 Human secreted proteins

IN Ruben, Steven M., Olney, MD, UNITED STATES  
Birse, Charles E., North Potomac, MD, UNITED STATES  
Duan, Roxanne D., Bethesda, MD, UNITED STATES  
Soppet, Daniel R., Centreville, VA, UNITED STATES  
Rosen, Craig A., Laytonsville, MD, UNITED STATES  
Shi, Yanggu, Gaithersburg, MD, UNITED STATES  
LaFleur, David W., Washington, DC, UNITED STATES  
Olsen, Henrik, Gaithersburg, MD, UNITED STATES  
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES  
Florence, Kimberly A., Rockville, MD, UNITED STATES  
Ni, Jian, Rockville, MD, UNITED STATES  
Young, Paul, Gaithersburg, MD, UNITED STATES  
PI US 2002028449 A1 20020307

AI US 2000-726643 A1 20001201 (9)  
RLI Continuation-in-part of Ser. No. WO 2000-US15187, filed on 2 Jun 2000,  
UNKNOWN  
PRAI US 1999-137725P 19990607 (60)  
DT Utility  
FS APPLICATION  
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850  
CLMN Number of Claims: 23  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 20287

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

L30 ANSWER 2 OF 11 USPATFULL

AN 2002:43671 USPATFULL  
TI 49 human secreted proteins  
IN Moore, Paul A., Germantown, MD, UNITED STATES  
Ruben, Steven M., Olney, MD, UNITED STATES  
Olsen, Henrik S., Gaithersburg, MD, UNITED STATES  
Shi, Yanggu, Gaithersburg, MD, UNITED STATES  
Rosen, Craig A., Laytonsville, MD, UNITED STATES  
Florence, Kimberly A., Rockville, MD, UNITED STATES  
Soppet, Daniel R., Centreville, VA, UNITED STATES  
LaFleur, David W., Washington, DC, UNITED STATES  
Endress, Gregory A., Potomac, MD, UNITED STATES  
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES  
Komatsoulis, George, Silver Spring, MD, UNITED STATES  
Duan, Roxanne D., Bethesda, MD, UNITED STATES

PI US 2002026040 A1 20020228

AI US 2001-904615 A1 20010716 (9)

RLI Continuation of Ser. No. US 2000-739254, filed on 19 Dec 2000, PENDING  
Continuation of Ser. No. US 2000-511554, filed on 23 Feb 2000, ABANDONED  
Continuation-in-part of Ser. No. WO 1999-US19330, filed on 24 Aug 1999,  
UNKNOWN

PRAI US 1998-97917P 19980825 (60)

US 1998-98634P 19980831 (60)

DT Utility

FS APPLICATION

LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 19401

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

L30 ANSWER 3 OF 11 USPATFULL

AN 2002:43668 USPATFULL

TI VASCULAR ENDOTHELIAL GROWTH FACTOR 3 ANTIBODIES

IN HU, JING-SHAN, SUNNYVALE, CA, UNITED STATES

OLSEN, HENRIK, GAITHERSBURG, MD, UNITED STATES

ROSEN, CRAIG A., LAYTONSVILLE, MD, UNITED STATES

PI US 2002026037 A1 20020228  
AI US 1999-244694 A1 19990210 (9)  
RLI Continuation-in-part of Ser. No. US 1998-132088, filed on 10 Aug 1998,  
ABANDONED Continuation-in-part of Ser. No. US 1998-33662, filed on 3 Mar  
1998, PENDING Division of Ser. No. US 1995-469641, filed on 6 Jun 1995,  
PENDING  
DT Utility  
FS APPLICATION  
LREP STERNE KESSLER GOLDSTEIN & FOX, 1100 NEW YORK AVENUE N W, SUITE 600,  
WASHINGTON, DC, 200053934  
CLMN Number of Claims: 25  
ECL Exemplary Claim: 1  
DRWN 5 Drawing Page(s)  
LN.CNT 6301

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a novel human protein called Vascular  
Endothelial Growth Factor 3, and isolated polynucleotides encoding this  
protein. Also provided are vectors, host cells, antibodies, and  
recombinant methods for producing this human protein. The invention  
further relates to diagnostic and therapeutic methods useful for  
diagnosing and treating disorders related to this novel human protein.

L30 ANSWER 4 OF 11 USPATFULL

AN 2002:43187 USPATFULL  
TI Transforming growth factor alpha HIII  
IN Wei, Ying-Fei, Berkeley, CA, UNITED STATES  
PI US 2002025553 A1 20020228  
AI US 2000-726348 A1 20001201 (9)  
RLI Continuation-in-part of Ser. No. US 1997-778545, filed on 3 Jan 1997,  
PENDING  
PRAI US 1996-11136P 19960104 (60)  
US 1999-168387P 19991202 (60)  
DT Utility  
FS APPLICATION  
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850  
CLMN Number of Claims: 25  
ECL Exemplary Claim: 1  
DRWN 5 Drawing Page(s)  
LN.CNT 11810  
AB The present invention relates to a novel human protein called  
Transforming Growth Factor Alpha III, and isolated polynucleotides  
encoding this protein. Also provided are vectors, host cells,  
antibodies, and recombinant methods for producing this human protein.  
The invention further relates to diagnostic and therapeutic methods  
useful for diagnosing and treating disorders related to this novel human  
protein.

L30 ANSWER 5 OF 11 USPATFULL

AN 2002:22131 USPATFULL  
TI 18 Human secreted proteins  
IN Shi, Yanggu, Gaithersburg, MD, UNITED STATES  
Young, Paul E., Gaithersburg, MD, UNITED STATES  
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES  
Soppet, Daniel R., Centreville, VA, UNITED STATES  
Ruben, Steven M., Olney, MD, UNITED STATES  
PI US 2002012966 A1 20020131  
AI US 2001-768826 A1 20010125 (9)  
RLI Continuation-in-part of Ser. No. WO 2000-US22350, filed on 15 Aug 2000,  
UNKNOWN  
PRAI US 1999-148759P 19990816 (60)  
DT Utility  
FS APPLICATION  
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850  
CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 18157

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

L30 ANSWER 6 OF 11 USPATFULL

AN 2001:155766 USPATFULL

TI 49 human secreted proteins

IN Moore, Paul A., Germantown, MD, United States  
Ruben, Steven M., Oley, MD, United States  
Olsen, Henrik S., Gaithersburg, MD, United States  
Shi, Yanggu, Gaithersburg, MD, United States  
Rosen, Craig A., Laytonsville, MD, United States  
Florence, Kimberly A., Rockville, MD, United States  
Soppet, Daniel R., Centreville, VA, United States  
Lafleur, David W., Washington, DC, United States  
Endress, Gregory A., Potomac, MD, United States  
Ebner, Reinhard, Gaithersburg, MD, United States  
Komatsoulis, George, Silver Spring, MD, United States  
Duan, Roxanne D., Bethesda, MD, United States

PI US 2001021700 A1 20010913

AI US 2000-739254 A1 20001219 (9)

RLI Continuation of Ser. No. US 2000-511554, filed on 23 Feb 2000, ABANDONED  
Continuation-in-part of Ser. No. WO 1999-US19330, filed on 24 Aug 1999,  
UNKNOWN

PRAI US 1998-97917P 19980825 (60)

US 1998-98634P 19980831 (60)

DT Utility

FS APPLICATION

LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 15462

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

L30 ANSWER 7 OF 11 USPATFULL

AN 2001:139293 USPATFULL

TI Fibroblast growth factor receptor-5

IN Young, Paul E., Gaithersburg, MD, United States  
Ruben, Steven M., Olney, MD, United States

PI US 2001016335 A1 20010823

AI US 2001-758386 A1 20010112 (9)

RLI Continuation of Ser. No. US 1999-293182, filed on 16 Apr 1999, ABANDONED

PRAI US 1998-105465P 19981023 (60)

DT Utility

FS APPLICATION

LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN 10 Drawing Page(s)

LN.CNT 6097

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to fibroblast growth factor receptor-5, a novel member of the fibroblast growth factor receptor family. The invention provides isolated nucleic acid molecules encoding human FGFR5 receptors. FGFR5 polypeptides are also provided, as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of FGFR5 receptor activity. Also provided are diagnostic methods for detecting disease states related to the aberrant expression of FGFR5 receptors. Further provided are therapeutic methods for treating disease states including, but not limited to, defects in wound healing, mucositis, defects in angiogenesis, ischemia, host defense dysfunction, endocrine dysfunction, disorders in immune function, and/or disorders in insulin secretion.

L30 ANSWER 8 OF 11 USPATFULL

AN 2001:111865 USPATFULL

TI Chitosan-based nitric oxide donor compositions

IN Smith, Daniel J., Stow, OH, United States  
Serhatkulu, Sibel, Akron, OH, United States

PA The University of Akron, Akron, OH, United States (U.S. corporation)

PI US 6261594 B1 20010717

AI US 1998-199732 19981125 (9)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Kulkosky, Peter F.

LREP Renner, Kenner, Greive, Bobak, Taylor & Weber

CLMN Number of Claims: 19

ECL Exemplary Claim: 1

DRWN 3 Drawing Figure(s); 3 Drawing Page(s)

LN.CNT 689

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A chitosan-based polymeric nitric oxide donor composition comprising a modified chitosan polymer and a nitric oxide [N2O2] dimer, wherein the nitric oxide [N2O2] dimer is bonded directly to the backbone of the modified chitosan polymer without further binding through a nucleophile residue or moiety. The chitosan-based polymeric nitric oxide donor composition is capable of site specific delivery and **controlled release** of nitric oxide under physiological conditions. The chitosan-based polymeric nitric oxide donor composition further provides a carrier having medically beneficial properties. A method is further included for preparing a chitosan-based polymeric nitric oxide donor composition comprising reacting a nitric oxide dimer (80-100 p.s.i.) with a modified chitosan polymer in the presence of sodium methoxide at room temperature. The chitosan-based polymeric nitric oxide composition can be incorporated into dry powder inhalers, wound dressings, implants, injectables, condoms, wound dressings and prosthesis coatings for use in a variety of medical applications in which an effective dosage of nitric oxide is indicated as a preferred method of treatment.

L30 ANSWER 9 OF 11 USPATFULL

AN 2001:14453 USPATFULL

TI Upregulation of Type III endothelial cell nitric oxide synthase by rho GTPase function inhibitors

IN Liao, James K., Weston, MA, United States

PA Brigham and Women's Hospital, Inc., Boston, MA, United States (U.S. corporation)

PI US 6180597 B1 20010130

AI US 1998-132849 19980811 (9)

RLI Continuation-in-part of Ser. No. US 1998-92618, filed on 5 Jun 1998, now abandoned

PRAI US 1998-78774P 19980319 (60)

DT Utility  
FS Granted  
EXNAM Primary Examiner: Russell, Jeffrey E.  
LREP Wolf, Greenfield & Sacks, P.C.  
CLMN Number of Claims: 93  
ECL Exemplary Claim: 1  
DRWN 27 Drawing Figure(s); 16 Drawing Page(s)  
LN.CNT 2725

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A use for rho GTPase function inhibitors is provided. In the instant invention, rho GTPase function inhibitors are found to upregulate endothelial cell Nitric Oxide Synthase activity. As a result, rho GTPase function inhibitors are useful in treating or preventing conditions that result from the abnormally low expression and/or activity of endothelial cell Nitric Oxide Synthase. Such conditions include pulmonary hypertension, ischemic stroke, impotence, heart failure, hypoxia-induced conditions, insulin deficiency, progressive renal disease, gastric or esophageal motility syndrome, etc. Subjects thought to benefit mostly from such treatments include nonhyperlipidemics and nonhypercholesterolemics, but do not necessarily exclude hyperlipidemics and hypercholesterolemics.

L30 ANSWER 10 OF 11 USPATFULL

AN 2000:153742 USPATFULL

TI Upregulation of Type III endothelial cell Nitric Oxide Synthase by HMG-CoA reductase inhibitors

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Endres, Matthias, Berlin, Germany, Federal Republic of  
Moskowitz, Michael A., Belmont, MA, United States

PA The General Hospital Corporation, Boston, MA, United States (U.S. corporation)  
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PI US 6147109 20001114

AI US 1998-132848 19980811 (9)

PRAI US 1997-62093P 19971014 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Jordan, Kimberly

LREP Wolf, Greenfield & Sacks, P.C.

CLMN Number of Claims: 54

ECL Exemplary Claim: 1

DRWN 18 Drawing Figure(s); 10 Drawing Page(s)

LN.CNT 1864

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A new use for HMG-CoA reductase inhibitors is provided. In the instant invention, HMG-CoA reductase inhibitors are found to upregulate endothelial cell Nitric Oxide Synthase activity through a mechanism other than preventing the formation of oxidative-LDL. As a result, HMG-CoA reductase inhibitors are useful in treating or preventing conditions that result from the abnormally low expression and/or activity of endothelial cell Nitric Oxide Synthase. Such conditions include pulmonary hypertension, ischemic stroke, impotence, heart failure, hypoxia-induced conditions, insulin deficiency, progressive renal disease, gastric or esophageal motility syndrome, etc. Subjects thought to benefit mostly from such treatments include nonhyperlipidemics and nonhypercholesterolemics, but not necessarily exclude hyperlipidemics and hypercholesterolemics.

L30 ANSWER 11 OF 11 USPATFULL

AN 2000:70640 USPATFULL

TI Antikinin compounds and uses thereof

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PI US 6071710 20000606  
AI US 1997-974735 19971119 (8)  
PRAI US 1996-31285P 19961120 (60)  
US 1997-64792P 19971110 (60)  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Kemmerer, Elizabeth; Assistant Examiner: Basi, Nirmal  
S.  
LREP Needle & Rosenberg, P.C.  
CLMN Number of Claims: 11  
ECL Exemplary Claim: 1  
DRWN 21 Drawing Figure(s); 12 Drawing Page(s)  
LN.CNT 1572

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An analog of the peptide consisting of RPPGF (SEQ ID NO:1) is provided. Mimetics of RPPGF (SEQ ID NO:1) and its retropeptide, FGPPR, are also provided. A peptide is provided having an antikinin activity and having the sequence X.sub.1 -R-P-P-G-F-X.sub.2 (SEQ ID NO:5), X.sub.1 -F-G-P-P-R-X.sub.2 (SEQ ID NO:7). Provided are methods of screening for a mimetic or analog of RPPGF (SEQ ID NO:1) or FGPPR (SEQ ID NO:2), screening for an RPPGF (SEQ ID NO:1) receptor, or screening for an antagonist of RPPGF (SEQ ID NO:1) or FGPPR (SEQ ID NO:2) is provided. Methods of treating conditions that can be treated by an antikinin activity and diseases that are associated with an antikinin activity are also provided.